UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

DATE: **May 14, 2013**
SUBJECT: **Mancozeb:** Revised Occupational and Residential Risk Assessment to Support Request for Section 3 Registrations on Walnuts.

PC Code: 014504	**DP Barcode:** D411769
Decision No.: NA	**Registration No.:** 70506-185, 70506-194, 70506-234, 70506-236
Petition No.: 1F7935	**Regulatory Action:** Section 3
Risk Assessment Type: Occupational/Residential Assessment	**Case No.:** 0643
TXR No.: NA	**CAS No.:** 8018-01-7
MRID No.: 44959602, 40312001, 40955401, 45937601, 44959603, 44959306	**40 CFR:** 180.176

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THROUGH: ExpoSAC Reviewer: Mathew Lloyd
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and,

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TO: Mary Waller, Risk Manager
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Note: This document supersedes the 11/04/12 memo D405401, *Mancozeb: Occupational and Residential Risk Assessment to Support Request for Section 3 Registrations on Walnuts.*

The Registration Division (RD) requested that the Health Effects Division (HED) conduct an exposure and risk assessment for proposed foliar uses of the active ingredient mancozeb on walnuts. This document addresses risks from exposure to mancozeb and mancozeb-derived

ethylenethiourea (ETU) to occupational pesticide handlers (mixers, loaders, applicators) and to workers at agricultural settings. The proposed uses will not result in residential exposure; however, the currently registered turf and home gardener uses have been reassessed in this document to reflect updates to HED's 2012 Residential SOPs. The residential exposures were revised since they will impact the aggregate assessment for mancozeb. It is HED policy to use the best available data to assess exposure. Several sources of generic data were used in this assessment as surrogate data in the absence of chemical-specific data, including**:** Pesticide Handlers Exposure Database Version 1.1 (PHED 1.1); the Agricultural Handler Exposure Task Force (AHETF) database; the Outdoor Residential Exposure Task Force (ORETF) database; the Agricultural Reentry Task Force (ARTF) database; the Residential SOPs (Lawns/Turf and Gardens and Trees sections), and other registrant-submitted exposure monitoring studies (MRIDs: 44959602, 40312001, 40955401, 45937601, 44959603, and 44959306). Some of these data are proprietary, and subject to the data protection provisions of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). **Note:** This memorandum was reviewed by the Exposure Science Advisory Committee (ExpoSAC) on November 8, 2012.

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1.0 EXECUTIVE SUMMARY

Mancozeb (a coordination product of zinc ion and manganese ethylene bisdithiocarbamate) is a member of the ethylene bisdithiocarbamate (EBDC) group of fungicides, which includes the related active ingredients maneb and metiram. Mancozeb is a broad-spectrum fungicide used in agriculture, professional turf management, and horticulture.

Proposed Use Profile

United Phosphorus, Inc. (UPI) submitted a petition to amend several mancozeb ai formulation labels (*i.e.*, Penncozeb Technical [EPA Reg. No.70506-188]; Penncozeb 75DF [EPA Reg. No. 70506-185]; Mancozeb 4FL Plowable Fungicide [EPA Reg. No. 70506-194]; Manzate Pro-Stick Fungicide [EPA Reg. No. 70506-234]; and Manzate Flowable [EPA Reg. No. 70506-236]) by adding a use on walnuts for the control of walnut blight, a bacterial disease caused by *Xanthomonas campestris pv. juglandis*.

The proposed use pattern and directions are similar for all mancozeb formulations for applications on walnuts. Ground and aerial foliar applications are permitted. The amended labels proposed a maximum single application rate of 1.8 pounds mancozeb per acre. The labels propose a maximum of ten applications per year and a Pre-Harvest Interval (PHI) of 75 days. Applications are to begin at early pre-bloom prior to or when catkins are partially expanded and additional applications can be made during bloom and early nutlet stage, or as needed if frequent rainfall occurs. The proposed labels require that mixers, loaders and applicators must wear: coveralls, long sleeved shirt, long pants, chemical resistant gloves (waterproof material), socks, and shoes. Mixers and loaders must also wear chemical resistant aprons and protective eyewear. It should be noted that no respiratory protection equipment (*e.g.,* respirators) is requested on the labels.

Exposure Profile

There is a potential for occupational exposure associated with handler activities (*i.e.*, mixing, loading, and applying) as well as with post-application activities (*i.e.*, re-entering treated areas). This document assesses the occupational exposures and risks for these newly proposed uses of the active ingredient (ai) mancozeb. Because ethylene thiourea (ETU) is an environmental degradate and metabolite of mancozeb, the hazards of both mancozeb and ETU have been assessed in this document. Based on application rate and label information, exposure is expected to occur for short- and intermediate-term durations. Chronic exposure is not expected for the proposed use patterns. Only inhalation exposures were considered for mancozeb because no effects were observed at the limit dose in a 28-day dermal rat study. In the case of ETU, however, inhalation and dermal exposures were considered for both the non-cancer and cancer risk assessments.

There are no proposed residential uses at this time; however, residential risks from mancozeb exposures have been assessed previously (D327307 & D327318; D. Davis, *et al.*, 6/11/07). An updated summary of the exposure and risk associated with the registered residential uses is provided for use in performing an aggregate exposure and risk assessment.

Mancozeb Hazard Concerns

Dermal toxicity endpoints were not identified for the short- and intermediate-term durations

because no dermal toxicity was observed at the limit dose in a 28-day dermal rat study. Short-term and intermediate-term inhalation risks for mancozeb are based on a point of departure (POD) from a 90-Day inhalation study in rats based on thyroid hyperplasia and decreased thyroxine (NOAEL of 21 mg/kg/day). Since the inhalation endpoint was not based on developmental effects, an 80 kg body weight was used when estimating risk. Risk estimate results for females 13 to 49 years old are also presented since the LOC for this particular lifestage population group is different. Acute oral, dermal and inhalation toxicities are classified as Toxicity Category IV. Mancozeb is a moderate eye irritant (Category III), a mild skin irritant (Category IV), and is not a skin sensitizer. The EPA's cancer concern for mancozeb is limited to risk from ethylenethiourea (ETU) which is both a metabolite and environmental degradate of mancozeb. The level of concern (LOC) for mancozeb occupational risk assessments for females 13-49 years old is 300, and 30 for males and females > 49 years old. Mancozeb dermal absorption is 1%, based on a dermal penetration study (MRID 44959602). Since no inhalation toxicity data are available, toxicity by the inhalation route is considered to be equivalent to toxicity by the oral route of exposure.

ETU Hazard Concerns

In addition to assessing risk from exposure to mancozeb, this assessment also considers risks from exposure to ETU, a metabolite and environmental degradate of mancozeb. ETU has been classified as a B2 carcinogen and is assessed for carcinogenic risk using a linear extrapolation approach with a Q1* of 6.01×10^{-2} $(mg/kg/day)^{-1}$. The Agency's LOC for ETU post-application risk assessments is 1000 (females 13-49 years old). Dermal absorption for ETU is 26% based on a rat dermal study (MRID 40312001). Since no inhalation toxicity data are available, toxicity by the inhalation route is considered to be equivalent to toxicity by the oral route of exposure. A body weight of 69 kg was used for assessing ETU non-cancer risks since the PODs are based on developmental effects. Since the dermal and inhalation routes of exposure are assessed using the same endpoint/POD, the exposures from these routes were combined to estimate a total (dermal + inhalation) risk estimate.

Occupational Exposure and Risk

Occupational Handlers Non-Cancer and Cancer Exposure and Risk Estimates for Mancozeb and ETU

Based on the proposed use, there is a potential for short- and intermediate-term occupational exposure to mancozeb during handling activities (*e.g.* mixing, loading, application).
All mixer/loader non-cancer risk scenarios do not exceed HED's level of concern (*i.e.*, MOEs ≥ 300 for females 13 to 49 years old and MOEs ≥ 30 for adult males and females>49 years old mancozeb inhalation exposures and MOEs ≥1000 for ETU combined dermal and inhalation exposures), at some level of risk mitigation (*e.g.*, gloves, respirators, or other engineering control measures).

Likewise, all application non-cancer risk scenarios do not exceed HED's level of concern at some level of risk mitigation *(e.g.,* gloves or other engineering control measures). Aerial and airblast applicator risks do not exceed HED's level of concern with engineering control measures (*i.e.,* enclosed cockpit or closed cab). Mixer/loader/applicators with mechanically pressurized handgun risks do not exceed HED's level of concern at label PPE (*i.e.,* gloves, no respirator).

The cancer risks from ETU exposure for all mixer/loading (M/L) scenarios for private handlers are estimated in the 10^{-6} to 10^{-8} range at label-specified PPE (*i.e.,* gloves, no respirator). Cancer risks for commercial handlers M/L scenarios ranged from 10^{-5} at label PPE, to 10^{-7} with additional PPE or mitigation measures (*i.e*. respirators, closed systems, or use of water soluble bags). The cancer risks for all application scenarios are estimated in the 10^{-6} (open cab airblast applications) to 10^{-8} (closed cab or cockpit for airblast and aerial applications respectively) range for both private and commercial handlers. The cancer risks for mixing/loading/application (M/L/A) scenarios are estimated in the 10^{-7} range for both private and commercial handlers at label PPE.

Occupational Post-Application Non-Cancer and Cancer Exposure and Risk Estimates

There is a potential for short- and intermediate-term occupational exposure during post-application activities. However, since there is no dermal endpoint identified up to the limit dose for mancozeb, only a dermal post-application assessment for ETU has been conducted.

The post-application occupational exposure scenarios assessed resulted in MOEs that do not exceed HED's level of concern (*i.e.*, ETU MOEs $\geq$ 1000) at the mancozeb current Restricted Entry Interval (REI) of 24 hours which is also proposed for walnut crops. The cancer risks estimates for post-application scenarios assessed are in the 10^{-7} to 10^{-8} range for private growers and 10^{-6} to 10^{-7} for commercial growers at Day 1 (*i.e.,* the 24 hour REI).

Based on the Agency's current practices, a quantitative non-cancer occupational post-application inhalation exposure assessment was not performed for mancozeb at this time. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative occupational post-application inhalation exposure assessment for mancozeb.

Restricted Entry Interval (REI)

The interim 24-hour restricted re-entry interval (REI) on the proposed labels is in compliance with the Worker Protection Standard (WPS) for agricultural pesticides and is consistent with previously approved REIs for registered formulations of mancozeb.

Residential Exposure and Risk

There are no proposed residential uses at this time; however, residential risks from mancozeb exposures have been assessed previously (D327307 & D327318; D. Davis, *et al.*, 6/11/07). Two residential uses that could result in mancozeb and ETU exposure (*i.e.,* home gardeners applying mancozeb to vegetables and golfers contacting mancozeb treated turf after application), have been reassessed in this document to reflect updates to HED's 2012 Residential SOPs[1] along with policy changes for body weight assumptions. A summary of the exposure and risk associated with the registered residential uses is provided for use in performing an aggregate exposure and risk assessment.

Residential Handlers Non-Cancer and Cancer Exposure and Risk Estimates for Mancozeb and ETU

1 Available: http://www.epa.gov/pesticides/science/residential-exposure-sop.html

Residential handler inhalation risk estimates from mancozeb exposures are not of concern (MOEs > 300). Inhalation MOEs range from 170,000 (mixing/loading/applying liquid formulation to vegetable gardens with backpack) to millions for manually pressurized handgun and hose-end sprayer applications. Residential handler risk estimates from ETU (combined dermal and inhalation) exposures are also not of concern (i.e., MOEs > 1000). MOEs range from 32,700 to 90,000. Residential handler estimated cancer risks were calculated for applicators using a backpack sprayer, manually pressurized and hose-end sprayer. The cancer risks for all M/L/A scenarios are estimated in the 10^{-8} range for residential handlers.

Post-application Non-Cancer Exposure and Risk Estimates for Residential Gardeners and Golfers
The quantitative exposure/risk assessment for residential post-application exposures is based on home gardeners applying mancozeb to vegetables and golfers contacting mancozeb treated turf after application. As no dermal hazard was identified for mancozeb, a quantitative dermal post-application assessment (non-cancer and cancer) was only performed for its metabolite, ETU. Inhalation exposures are not expected for the post-application activities. Post application non-cancer risks estimates from mancozeb-derived ETU for adults and youth exposed to treated home gardens on Day 0 (the day of application) do not exceed HED's LOC (*i.e.,* MOE ≥ 1000 for adults and MOE ≥ 100 for youth) and, therefore; are not of concern. Residential post-application risk estimates were assessed for adult and youth golfers contacting mancozeb treated turf after application. There are no post-application short-term risk estimates of concern for youth or adults golfers exposed to ETU from contact with mancozeb treated golf courses.

Post-application Cancer Exposure and Risk Estimates for ETU from Mancozeb
Post-application cancer risks for adult home gardeners are estimated in the 10^{-7} range. The cancer risk to adult golfers from exposure to mancozeb-derived ETU is estimated in the 10^{-8} range.

Human Studies Review
This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. These data, which include studies from the Pesticide Handlers Exposure Database Version 1.1 (PHED 1.1); the Agricultural Handler Exposure Task Force (AHETF) database; the Outdoor Residential Exposure Task Force (ORETF) database; the Agricultural Re-entry Task Force (ARTF) database; and other registrant-submitted studies; (1) are subject to ethics review pursuant to 40 CFR 26, (2) have received that review, and (3) are compliant with applicable ethics requirements. For certain studies that review may have included review by the Human Studies Review Board. Descriptions of data sources as well as guidance on their use can be found at the Agency website.[2]

2.0 SUMMARY OF CONCLUSIONS AND DATA REQUIREMENTS

Occupational exposure scenarios assessed resulted in MOEs that do not exceed HED's level of concern (*i.e.*, MOEs ≥ 300 for females 13 to 49 years old and MOEs ≥ 30 for adult males and females>49 years old) for mancozeb inhalation exposures and MOEs ≥1000 for ETU combined

2 http://www.epa.gov/pesticides/science/handler-exposure-data.html and http://www.epa.gov/pesticides/science/post-app-exposure-data.html

dermal and inhalation exposures), at some level of risk mitigation (*e.g.,* gloves, respirators, or other engineering control measures). All mixer/loader scenarios do not exceed HED's level of concern (*i.e.*, MOEs ≥ 300 for mancozeb exposures and MOEs ≥1000 for ETU exposures), at some level of risk mitigation (*e.g.,* gloves, respirators, or other engineering control measures). Non-cancer risks estimates for mixer/loader scenarios using dry flowable (DF) formulations in support of aerial applications exceed HED's level of concern (*i.e.,* MOE=260 for mancozeb inhalation exposures and MOE=750 for ETU exposures) at label PPE (*i.e.,* gloves, no respirator). It should be noted that no respiratory protection equipment or other engineering control measures are requested on the DF labels. **The proposed labels should be amended to include additional mitigation measures (*e.g.,* respirators, or other engineering control measures) as needed.**

3.0 HAZARD CHARACTERIZATION

Mancozeb was first registered in the United States in 1948 as a broad spectrum fungicide used in agriculture, professional turf management, and horticulture. Mancozeb is a member of the ethylene bisdithiocarbamate (EBDC) group of fungicides, which includes the related active ingredients maneb and metiram. The EBDCs share the common degradate ethylene thiourea (ETU), which has been considered in the Agency's assessments. Similar to other EBDCs, the thyroid is the target organ for mancozeb and ETU. Thyroid effects were observed in multiple studies across species. Thyroid toxicity was manifested as alterations in thyroid hormones, increased thyroid weight, and microscopic thyroid lesions (mainly thyroid follicular cell hyperplasia), and thyroid tumors.[3] Ethylene thiourea (ETU) is produced through degradation of mancozeb during spray mix preparation, during spray application and in the environment (*e.g.,* on treated leaves) after application. Tank mix stability studies submitted to, and reviewed by, the Agency in 1991 indicated that 0.1 percent of the mancozeb parent converted to ETU during mixing/loading and 0.2 percent converted to ETU during application (D327307 & D327318; D. Davis, 6/11/07). Post-application assessments were based on empirical measures of ETU in dislodgeable foliar residue dissipation studies.

ETU is a carcinogen with a Q1* ($0.0601\ (mg/kg/day)^{-1}$). Because mancozeb is known to be converted to ETU, it has also been classified as Group B2 for carcinogenicity, and the ETU cancer potency factor is used for assessing cancer risk associated from mancozeb uses. All cancer assessments are based only on the presence of ETU residues. The hazard characterizations for both mancozeb and ETU are briefly summarized below.

3.1 Mancozeb Hazard Concerns

Similar to other EBDCs, the thyroid is the primary target organ for mancozeb. Dermal toxicity endpoints were not identified for the short- and intermediate-term durations (no dermal toxicity observed at the limit dose of 1000 mg/kg/day) in a 28-day dermal toxicity study in the rat. Therefore, no assessment was conducted for short-term and intermediate-term dermal exposures. Based on the proposed use pattern, chronic exposures are not anticipated; therefore, only short-term and intermediate-term inhalation risk exposures were assessed for occupational scenarios.

[3] Mancozeb Facts, U.S. Environmental Protection Agency, OPP, 738-F-05-XX, September 2005.

Mancozeb caused thyroid toxicity in a number of different studies and species. The thyroid toxicity is caused by inhibition of thyroid peroxidase by the mancozeb metabolite, ETU. Mancozeb also caused a number of very severe malformations in the rat developmental study. These malformations were caused by ETU, for which there are many developmental studies reported in the literature. Neuromuscular toxicity was caused by mancozeb, but not by ETU.

Thyroid hormones are critical for normal brain development and data are needed about the sensitivity of the fetus and young animals. A developmental thyroid study is presently being conducted with ETU because it is the ultimate thyroid toxicant. Information from this study could affect the mancozeb endpoints and the mancozeb risk assessment therefore has a database uncertainty factor of 10X applied to Females 13-49 years old and to children < 6 years old. Because adult humans are less sensitive than rats to thyroid toxicity, the interspecies uncertainty factor for thyroid toxicity was reduced from 10X to 3X. The combination of different endpoints and uncertainty factors for different population groups resulted in a more extensive endpoint table than is usually the case. Summaries of acute toxicity and toxicity endpoints for mancozeb are shown in Tables 1, 2 and 3.

Acute Toxicity

Table 1. Acute Toxicity Profile for Mancozeb				
Guideline Number	**Study Type**	**MRID Number**	**Results**	**Toxicity Category**
870.1100	Acute oral	00142522	LD_{50} >5000 mg/kg	IV
870.1200	Acute dermal	00142522	LD_{50} > 5000 mg/kg	IV
870.1300	Acute inhalation	00142522	LD_{50} >5.14 mg/L	IV
870.2400	Primary eye irritation	00142522	Corneal damage < 7 days	III
870.2500	Primary skin irritation	00142522	Negative	IV
870.2600	Dermal sensitization	40469501	Negative	NA[a]
870.6200	Acute neurotoxicity	47126201	NOAEL = 500 mg/kg LOAEL = 1000 mg/kg (decreased motor activity)	NA

a NA = Not Applicable

Toxicological PODs Used for Risk Assessment

Table 2. Summary of Toxicological Doses and Endpoints for Mancozeb for Use in Occupational Risk Assessments				
Exposure/ Scenario	**Point of Departure**	**Uncertainty Factors**	**Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Mancozeb Occupational Dermal Exposure				
Dermal (Short-, and Intermediate-Term, all pop. subgroups)	Risk Assessment not required. No systemic toxicity via the dermal route at 1000 mg/kg/day and there are no developmental or reproductive concerns at systemic doses which would occur as a result of dermal exposures from registered uses			
Mancozeb Occupational Inhalation[2] Exposure (all durations)				

Table 2. Summary of Toxicological Doses and Endpoints for Mancozeb for Use in Occupational Risk Assessments				
Exposure/ Scenario	**Point of Departure**	**Uncertainty Factors**	**Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Inhalation (Adult Males, Females >49 years)	NOAEL = 0.079 mg/L [21 mg/kg/day]	UF_A= 3x UF_H = 10x	LOC = 30	Subchronic Inhalation in the rat LOAEL = 0.326 mg/L based on thyroid toxicity
Inhalation (Females 13-49 years)	NOAEL = 0.079 mg/L [21 mg/kg/day]	UF_A= 3x UF_H = 10x UF_{DB} = 10x	LOC = 300	Subchronic Inhalation in the rat LOAEL = 0.326 mg/L based on thyroid toxicity
Mancozeb Cancer				
Cancer (all routes)	Mancozeb's potential for carcinogenicity is due to the formation of the metabolite, ETU, which is classified as a probable human carcinogen (B2). Mancozeb's cancer risk is calculated by estimating exposure to mancozeb-derived ETU and using the ETU cancer potency factor (Q_1^*) of 6.01 x 10^{-2} $(mg/kg/day)^{-1}$ provide a quantitative estimate of risk.			

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). UF_L = use of a LOAEL to extrapolate a NOAEL. UF_{DB} = to account for the absence of key data (*i.e.*, lack of a critical study). MOE = margin of exposure. LOC = level of concern. N/A = not applicable.

1. Mancozeb dermal absorption factor (DA) is 1% based on a dermal penetration study (MRID40955401).
2. Since no inhalation absorption data are available, toxicity by the inhalation route is considered to be equivalent to the estimated toxicity by the oral route of exposure, therefore, mancozeb Inhalation absorption factor (IA) is 100%.

Table 3. Summary of Toxicological Doses and Endpoints for Mancozeb for Use in Residential Risk Assessments				
Exposure/ Scenario	**Point of Departure**	**Uncertainty Factors**	**Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Mancozeb Incidental Oral Exposure				
Incidental Oral (Children < 6 years of age)	NOAEL = 9.24 mg/kg/day	UF_A= 3x UF_H = 10x FQPA UF_{DB} = 10x	LOC = 300	Subchronic Toxicity Study in the rat. LOAEL = 17.82 mg/kg/day based on decreased thyroxine
Mancozeb Residential Dermal Exposure				
Dermal (Short-, and Intermediate-Term, all pop. subgroups)	Risk Assessment not required. No systemic toxicity via the dermal route at 1000 mg/kg/day and there are no developmental or reproductive concerns at systemic doses which would occur as a result of dermal exposures from registered uses (dermal absorption[1]; DA= 1%)			
Mancozeb Residential Inhalation[2] Exposure (all durations)				
Inhalation (Adult Males, Females >49 years, and Children ≥ 6 years)	NOAEL = 0.079 mg/L (21 mg/kg/day)	UF_A= 3x UF_H = 10x FQPA SF = 1x	LOC = 30	Subchronic Inhalation in the rat LOAEL = 0.326 mg/L based on thyroid toxicity

Table 3. Summary of Toxicological Doses and Endpoints for Mancozeb for Use in Residential Risk Assessments				
Exposure/ Scenario	**Point of Departure**	**Uncertainty Factors**	**Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Inhalation (Females 13-49 years and Children < 6 years)	NOAEL = 0.079 mg/L (21 mg/kg/day)	UF_A= 3x UF_H = 10x FQPA UF_{DB} = 10x	LOC = 300	Subchronic Inhalation in the rat LOAEL = 0.326 mg/L based on thyroid toxicity
Mancozeb Cancer				
Cancer (all routes)	Mancozeb's potential for carcinogenicity is due to the formation of the metabolite, ETU, which is classified as a probable human carcinogen (B2). Mancozeb's cancer risk is calculated by estimating exposure to mancozeb-derived ETU and using the ETU cancer potency factor (Q_1^*) of 6.01 x 10^{-2} $(mg/kg/day)^{-1}$ to provide a quantitative estimate of risk.			

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). UF_L = use of a LOAEL to extrapolate a NOAEL. UF_S = use of a short-term study for long-term risk assessment. UF_{DB} = to account for the absence of key data (*i.e.*, lack of a critical study). MOE = margin of exposure. LOC = level of concern. N/A = not applicable.
1. Mancozeb dermal absorption factor (DA) is 1% based on a dermal penetration study (MRID40955401).
2. Since no inhalation absorption data are available, toxicity by the inhalation route is considered to be equivalent to the estimated toxicity by the oral route of exposure, therefore; mancozeb Inhalation absorption factor (IA) is 100%.

3.2 Ethylene Thiourea Hazard Concerns

Ethylene thiourea (ETU) is an environmental degradate of mancozeb which can form during the application process in spray mixes or subsequently on treated foliage. Tank mix stability studies submitted to, and reviewed by, the Agency in 1991 indicated that 0.1 percent of the mancozeb parent converted to ETU during mixing/loading and 0.2 percent converted to ETU during application (D327307 & D327318; D. Davis, 6/11/07). ETU residues also occur on treated foliage to which field workers may be exposed and these are determined empirically in monitoring studies.

Approximately 7.5% of parent EBDC is metabolized to ETU in the body[4]. The ETU formed from the *in vivo* metabolism of parent EBDC is added to the ETU to which people are exposed as a degradate (direct exposure) to determine a total ETU absorbed dose.

HED has relied on a combination of guideline data and several studies in the open literature to assess hazard for ETU. ETU is not acutely toxic via the dermal or inhalation routes of exposure. There are no data on acute oral toxicity. ETU is not a skin or eye irritant.

ETU causes thyroid toxicity in a number of different studies and species by inhibition of thyroid

[4] A. Kocialski, 09/12/1989. Memo: *Establishment of an in-vivo Metabolic Conversion Factor of 7.5%for all Ethylene Bis(Dithio) Carbamates (EBDCS)when Converting EBDCSs to Ethylene Thiourea (ETU) in- vivo.*

peroxidase. ETU also caused many severe malformations in rat studies which are reported in the literature. Repeated dosing is not necessary, and the malformations have been observed after a single dose of ETU, which was very close to the dose for repeated dosing.

Thyroid hormones are critical for normal brain development and data are needed about the sensitivity of the fetus and young animals. A developmental thyroid study is presently being conducted with ETU. There is a database uncertainty factor of 10X applied to Females 13-49 years old and to children < 6 years old.

Toxicological PODs Used for Risk Assessment

The toxicological endpoints used to complete occupational and residential risk assessments for ETU are listed in Tables 4 and 5.

Table 4. Summary of Toxicological Doses and Endpoints for ETU for Use in Occupational Risk Assessments

Exposure/ Scenario	Exposure/ Scenario	Exposure/ Scenario	Exposure/ Scenario	Exposure/ Scenario
ETU Occupational Dermal[1] Exposure				
Dermal (Short and Intermediate-Term) (Adult Males, Females >49 years)	NOAEL= 7 mg/kg/day	UF_A= 10x UF_H=10x	LOC = 100	4-week range-finding dog study LOAEL= 34 mg/kg/day based on thyroid toxicity
Dermal (Short and Intermediate-Term) (Females 13-49 years old)	NOAEL= 5 mg/kg/day	UF_A= 10x UF_H=10x UF_{DB} = 10x	LOC = 1000	Developmental Rat Toxicity (Khera Study, MRID No. 45937601) LOAEL = 10 mg/kg/day, based on hydrocephaly and other malformations
ETU Occupational Inhalation [2] Exposure				
Inhalation (Short and Intermediate-Term) (Adult Males, Females >49 years)	NOAEL= 7 mg/kg/day	UF_A= 10x UF_H=10x	LOC = 100	4-week range-finding dog study LOAEL= 34 mg/kg/day based thyroid toxicity
Inhalation (Short and Intermediate-Term) (Females 13-	NOAEL= 5 mg/kg/day	UF_A= 10x UF_H=10x UF_{DB} = 10x	LOC = 1000	Developmental Rat Toxicity (Khera Study, MRID No. 45937601) LOAEL = 10 mg/kg/day, based on hydrocephaly and other malformations

Table 4. Summary of Toxicological Doses and Endpoints for ETU for Use in Occupational Risk Assessments				
Exposure/ Scenario	**Exposure/ Scenario**	**Exposure/ Scenario**	**Exposure/ Scenario**	**Exposure/ Scenario**
49 years old)				
ETU Cancer [3]				
Cancer (all routes)	Q_1^* = 6.01 x 10^{-2} $(mg/kg/day)^{-1}$	ETU is classified as a **Group B2** carcinogen with a linear low-dose extrapolation approach for human risk assessment based on liver tumors in female mice.		

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). UF_L = use of a LOAEL to extrapolate a NOAEL. UF_S = use of a short-term study for long-term risk assessment. UF_{DB} = to account for the absence of key data (*i.e.*, lack of a critical study). MOE = margin of exposure. LOC = level of concern. N/A = not applicable.

1. ETU dermal absorption factor (DA) is 26 % based on a rat dermal study (MRID 40312001)
2. Since no inhalation absorption data are available, toxicity by the inhalation route is considered to be equivalent to the estimated toxicity by the oral route of exposure, therefore, ETU's Inhalation absorption factor (IA) is 100%.
3. ETU has also been classified as a probable human carcinogen B2 carcinogen and is assessed for carcinogenic risk using a linear extrapolation approach with a Q_1^* of 6.01 x 10^{-2} $(mg/kg/day)^{-1}$. The cancer risk estimates are presented based on the Q_1^* value for OPP risk managers to evaluate and mitigate as needed.

Table 5. Summary of Toxicological Doses and Endpoints for ETU for Use in Residential Risk Assessments				
Exposure/ Scenario	**Exposure/ Scenario**	**Exposure/ Scenario**	**Exposure/ Scenario**	**Exposure/ Scenario**
ETU Incidental Oral Exposure				
Incidental Oral Short and Intermediate-Term (Children < 6 years of age)	NOAEL= 7 mg/kg/day	UF_A= 10x UF_H=10x FQPA UF_{DB} = 10x	LOC = 1000	4-week range-finding dog study LOAEL= 34 mg/kg/day based on thyroid toxicity
ETU Residential Dermal [1] Exposure				
Dermal (Short and Intermediate-Term) (Children < 6 years of age)	NOAEL= 7 mg/kg/day	UF_A= 10x UF_H=10x FQPA UF_{DB} = 10x	LOC = 1000	4-week range-finding dog study LOAEL= 34 mg/kg/day based on thyroid toxicity

Table 5. Summary of Toxicological Doses and Endpoints for ETU for Use in Residential Risk Assessments				
Exposure/ Scenario	**Exposure/ Scenario**	**Exposure/ Scenario**	**Exposure/ Scenario**	**Exposure/ Scenario**
Dermal (Short and Intermediate-Term) (Adult Males, Females >49 years, Children ≥ 6 years)	NOAEL= 7 mg/kg/day	UF_A= 10x UF_H=10x FQPA SF= 1x	LOC = 100	4-week range-finding dog study LOAEL= 34 mg/kg/day based on thyroid toxicity
Dermal (Short and Intermediate-Term) (Females 13-49 years old)	NOAEL= 5 mg/kg/day	UF_A= 10x UF_H=10x FQPA UF_{DB} = 10x	LOC = 1000	Developmental Rat Toxicity (Khera Study, MRID No. 45937601) LOAEL = 10 mg/kg/day, based on hydrocephaly and other malformations
ETU Residential Inhalation [2] Exposure				
Inhalation (Short and Intermediate-Term) (Children < 6 years of age)	NOAEL= 7 mg/kg/day	UF_A= 10x UF_H=10x FQPA UF_{DB} = 10x	LOC = 1000	4-week range-finding dog study LOAEL= 34 mg/kg/day based thyroid toxicity
Inhalation (Short and Intermediate-Term) (Adult Males, Females >49 years, Children ≥ 6 years)	NOAEL= 7 mg/kg/day	UF_A= 10x UF_H=10x FQPA SF= 1x	LOC = 100	4-week range-finding dog study LOAEL= 34 mg/kg/day based thyroid toxicity
Inhalation (Short and Intermediate-Term) (Females 13-49 years old)	NOAEL= 5 mg/kg/day	UF_A= 10x UF_H=10x FQPA UF_{DB} = 10x	LOC = 1000	Developmental Rat Toxicity (Khera Study, MRID No. 45937601) LOAEL = 10 mg/kg/day, based on hydrocephaly and other malformations
ETU Cancer				
Cancer [3] (all routes)	Q_1^* = 6.01 x 10^{-2} $(mg/kg/day)^{-1}$	ETU is classified as a **Group B2** carcinogen with a linear low-dose extrapolation approach for human risk assessment based on liver tumors in female mice.		

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity

among members of the human population (intraspecies). UF_L = use of a LOAEL to extrapolate a NOAEL. UF_S = use of a short-term study for long-term risk assessment. UF_{DB} = to account for the absence of key data (*i.e.*, lack of a critical study). MOE = margin of exposure. LOC = level of concern. N/A = not applicable.
1. ETU dermal absorption factor (DA) is 26 % based on a rat dermal study (MRID 40312001)
2. Since no inhalation absorption data are available, toxicity by the inhalation route is considered to be equivalent to the estimated toxicity by the oral route of exposure, therefore; ETU's Inhalation absorption factor (IA) is 100%.
3. ETU has also been classified as a probable human carcinogen B2 carcinogen and is assessed for carcinogenic risk using a linear extrapolation approach with a Q_1* of 6.01×10^{-2} $(mg/kg/day)^{-1}$ The cancer risk estimates are presented based on the Q_1* value for OPP risk managers to evaluate and mitigate as needed.

4.0 REGISTERED AND PROPOSED USE PATTERNS

Mancozeb is a widely used contact fungicide in agriculture, professional turf management, horticulture, and home gardening. Mancozeb formulations include wettable powders, dry flowables, liquid flowables and dusts. The product is currently registered for foliar application and seed treatment on various agricultural crops. Agricultural uses include pome fruit crops (*e.g.*, apples, pears), fruits and vegetables (*e.g.*, cucumbers, onions, tomatoes, and grapes), some row crops (*e.g.*, corn and potatoes), seed piece treatment (*e.g.* potatoes) and seed treatment (*e.g.* rice, wheat and cotton). Horticultural uses include ornamental plants in nurseries and greenhouses, sod farms, and golf courses.

The petitioner has proposed to amend the use pattern for various mancozeb formulations (*i.e.*, Penncozeb Technical [EPA Reg. No.70506-188]; Penncozeb 75DF [EPA Reg. No. 70506-185]; Penncozeb 4FL Plowable Fungicide [EPA Reg. No. 70506-194]; Manzate Pro-Stick Fungicide, [EPA Reg. No. 70506-234]; and Manzate Flowable [EPA Reg. No. 70506-236] adding a use on walnuts for the control of walnut blight, a bacterial disease caused by *Xanthomonas campestris pv. juglandis*.

The proposed use pattern and directions are similar for all mancozeb formulations for applications on walnuts. Ground and aerial foliar applications are permitted. The maximum single application rate proposed is 1.8 pounds mancozeb per acre. The labels propose a maximum of ten applications per year (*i.e.,* maximum total application rate of 18 lb ai/year), and a Pre-Harvest Interval (PHI) of 75 days. Applications are to begin at early pre-bloom prior to or when catkins are partially expanded and additional applications can be made during bloom and early nutlet stage, or as needed if frequent rainfall occurs. The proposed labels require that occupational handlers wear long-sleeve shirt and long pants, chemical resistant gloves, chemical resistant footwear plus socks. It should be noted that no respiratory protection equipment (*e.g.,* respirators) is requested on the labels.

A use profile for the mancozeb formulations on walnuts is summarized in Table 6.

Table 6. Summary of Directions for Use of Mancozeb

Applic. Timing, Type, and Equip.	Formulation [EPA Reg. No.]	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Applic. Rate/Year (lb ai/A)	PHI (days)	Use Directions and Limitations
Walnuts						
Ground, Aerial Foliar Applications	WDG 75% ai [70506-234] DF 75 %ai	1.8	10 applications /year	18	75 days	Begin applications at early pre-bloom prior to or when catkins are partially expanded.

Table 6. Summary of Directions for Use of Mancozeb						
Applic. Timing, Type, and Equip.	**Formulation [EPA Reg. No.]**	**Applic. Rate (lb ai/A)**	**Max. No. Applic. per Season**	**Max. Applic. Rate/Year (lb ai/A)**	**PHI (days)**	**Use Directions and Limitations**
	[70506-185] FLC 37% ai [70506-194, 70506-236]					Make additional applications during bloom and early nutlet stage, or as needed if frequent rainfall occurs.

WDG- Water Dispersible Granules
DF- Dry Flowable
FLC- Flowable Liquid Concentrate

5.0 OCCUPATIONAL EXPOSURE AND RISK ESTIMATES

Occupational handler exposure to mancozeb is expected for individuals involved in foliar applications to walnuts (*i.e.*, during mixing, loading, and applying). Agricultural workers performing post-application activities such as scouting, irrigation, transplanting, and harvesting are also expected to receive exposure to mancozeb and mancozeb-derived ETU residues.

5.1 Occupational Handler Exposure/Risk Estimates

HED uses the term handlers to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct job functions or tasks related to applications and exposures can vary depending on the specifics of each task. Job requirements (amount of chemical used in each application), the kinds of equipment used, the target being treated, and the level of protection used by a handler can cause exposure levels to differ in a manner specific to each application event.

Based on the anticipated use patterns and current labeling, types of equipment and techniques that can potentially be used, occupational handler exposure is expected from the proposed uses. The quantitative exposure/risk assessment developed for occupational handlers is based on the following scenarios:

1. Mixer/Loader using open pouring of liquids in support of aerial, and airblast operations;
2. Mixer/Loader using dry flowable and water dispersible granules in support of aerial and airblast operations;
3. Aerial Applicators (enclosed cockpit);
4. Applicators using airblast equipment; and
5. Mixer/loader/applicator with mechanically pressurized handgun.

Although flagger scenarios are normally considered for aerial application, they are not considered for mancozeb because the label prohibits the use of human flaggers. As stated on the labels, mixers, loaders and applicators must wear: coveralls, long sleeved shirt, long pants, chemical

resistant gloves (waterproof material), socks, and shoes. Mixers and loaders must also wear chemical resistance aprons and protective eyewear. It should be noted that no respiratory protection equipment (*e.g.,* respirators) is requested on the labels.

Handler exposure is expected to be short- or intermediate-term based on information provided on the proposed label. Chronic exposure is not expected for the proposed use patterns. The proposed use pattern is summarized in Table 6.

Only inhalation MOEs were calculated for short/intermediate term mancozeb exposures because no effects were observed in mancozeb 28 day dermal toxicity study. Risk calculations were also performed to assess the risk of ETU, a degradate in the mancozeb spray mix, which is metabolized from absorbed mancozeb.

Occupational Handler Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the occupational handler risk assessments. Each assumption and factor is detailed below on an individual basis.

Application Rate:
The maximum proposed application rates were used (*i.e.,* 1.8 lb ai/acre and 0.018 lb ai/gallon). Tank mix stability studies submitted to, and reviewed by, the Agency in 1991 indicated that 0.1 percent of the mancozeb parent converted to ETU during mixing/loading and 0.2 percent converted to ETU during application (D327307 & D327318; D. Davis, 6/11/07).

Unit Exposures:
It is the policy of HED to use the best available data to assess handler exposure. Sources of generic handler data, used as surrogate data in the absence of chemical-specific data, include PHED 1.1, the AHETF database, the Outdoor Residential Exposure Task Force (ORETF) database, or other registrant-submitted occupational exposure studies. Some of these data are proprietary (e.g., AHETF data), and subject to the data protection provisions of FIFRA. The standard values recommended for use in predicting handler exposure that are used in this assessment, known as "unit exposures", are outlined in the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table [5]", which, along with additional information on HED policy on use of surrogate data, including descriptions of the various sources, can be found at the Agency website[6].

Estimates of dermal and inhalation exposure were calculated for various levels of personal protective equipment (PPE). Results are presented for "baseline," defined as a single layer of clothing consisting of a long sleeved shirt, long pants, shoes plus socks, no protective gloves, and no respirator, as well as baseline with various levels of PPE as necessary (*e.g.,* gloves, respirator, etc). The mancozeb product labels require that mixers, loaders and applicators must wear: coveralls, long sleeved shirt, long pants, chemical resistant gloves (waterproof material), socks, and shoes. Mixers and loaders must also wear chemical resistant aprons and protective eyewear. It

5 Available: http://www.epa.gov/opp00001/science/handler-exposure-table.pdf
6 Available: http://www.epa.gov/pesticides/science/handler-exposure-data.html

should be noted that no respiratory protection is required.

Area Treated or Amount Handled
Based on HED ExpoSAC Policy No. 9.1, the area treated in a day was assumed to be:

- 350 acres for mixing/loading to support aerial applications,
- 40 acres for mixing/loading to support airblast applications
- 350 acres for applying with aerial equipment
- 40 acres for applying with airblast equipment,
- 1000 gallons for mixing/loading/applying with mechanically-pressurized handgun,

Body Weight

- The standard body weight for the general population (80 kg) was used for assessing mancozeb inhalation non-cancer risks and ETU cancer risks since the endpoints selected were not developmental and/or fetal effects.
- A body weight of 69 kg was used for assessing ETU non-cancer risks since the POD are based on developmental and/or fetal effects.
- Risk estimate results for two population sub-groups *(i.e*., females 13 to 49 years old, and males and females>49 years old) are presented since the LOCs for these lifestage population groups are different.

Absorption Factors
Even though there is no dermal hazard assessed for mancozeb, a dermal absorption factor (DAF) is still required and used in the assessment. The 1% DAF is relevant for manzozeb because a metabolic conversion factor of 7.5 % [7] of the absorbed mancozeb dose is used to calculate the ETU dose due to in-vivo metabolism. A dermal absorption factor of 26 %was used for ETU. A Since no inhalation absorption data are available, toxicity by the inhalation route is considered to be equivalent to the estimated toxicity by the oral route of exposure (100%).

Exposure Duration:
HED classifies exposures from 1 to 30 days as short-term and exposures 30 days to six months as intermediate-term. Exposure duration is determined by many things, including the exposed population, the use site, the pest pressure triggering the use of the pesticide, and the cultural practices surrounding that use site. For most agricultural uses, it is reasonable to believe that occupational handlers will not apply the same chemical every day for more than a one-month time frame; however, there may be a large agribusiness and/or commercial applicators who may apply a product over a period of weeks (*e.g.*, completing multiple applications for multiple clients within a region).

Handler exposure is expected to be short- or intermediate-term based on information provided on the proposed label. Chronic exposure is not expected for the proposed use patterns.

Mitigation/Personal Protective Equipment:
Occupational handler exposure assessments are completed by HED using different levels of risk

[7] A. Kocialski, 09/12/1989. Memo: *Establishment of an in-vivo Metabolic Conversion Factor of 7.5%for all Ethylene Bis(Dithio) Carbamates (EBDCS)when Converting EBDCSs to Ethylene Thiourea (ETU) in- vivo.*

mitigation. Typically, HED uses a tiered approach. The lowest tier is designed as the baseline exposure scenario (*i.e.,* long-sleeve shirt, long pants, shoes, socks, no respirator). If risk estimates are of concern at baseline attire, then increasing levels of PPE (*i.e.,* gloves, respirators) are evaluated. If risk estimates remain a concern with maximum PPE, then engineering controls (*i.e.,* enclosed cabs or cockpits, water-soluble packaging, and closed mixing/loading systems) are evaluated. This approach is used to ensure that the lowest level of risk mitigation that provides adequate protection is selected, since the addition of PPE and engineering controls involves an additional expense to the user and (in the case of PPE) also involves an additional burden to the user due to decreased comfort and dexterity and increased heat stress and respiratory stress.

Days per year of Exposure
To assess cancer risk, it is assumed that private growers would be exposed 10 days per year and commercial applicators would be exposed 30 days per year. The term "private grower" means that the grower or one of the workers would apply the pesticides to land owned or operated by the grower. "Commercial applicators" are assumed to complete multiple applications for multiple clients.

Years per Lifetime of Exposure: It is assumed that handlers would be exposed for 35 years out of a 78 year lifespan.

Lifetime Expectancy: Life expectancy values are from the Exposure Factors Handbook 2011 Edition Table 18-1 (U.S. EPA, 2011). The table shows that the overall life expectancy is 78 years based on life expectancy data from 2007. In 2007, the average life expectancy for males was 75 years and 80 years for females. Based on the available data, the recommended value for use in cancer risk assessments is 78 years.

Occupational Handler Non-Cancer Exposure and Risk Estimate Equations

Mancozeb potential daily exposures for occupational handlers were calculated using the following formulas:

*Daily Exposure (mg ai /day) = UE (µg ai / lb ai) * AR (lb ai /A) * AT (A /day) * 1E-3 mg/µg*

where:
Daily Exposure = Amount (mg ai/day) that is available for dermal or inhalation absorption,
UE = Unit Exposure (µg ai / lb ai),
AR = maximum application rate according to proposed label (lb ai /A), and
AT = daily acres treated (A /day).

The daily doses were calculated using the following formula:

$$\textit{Average Daily Dose (mg ai/kg/day)} = \frac{\textit{[Daily Exposure (mg ai/day) * Absorption (\%)]}}{\textit{Body Weight (kg)}}$$

where:
Average Daily Dose = Absorbed dose received from exposure to a pesticide in a given scenario (mg pesticide active ingredient/kg body weight/day),
Daily Exposure = Amount (mg ai/day) that is available for dermal or inhalation absorption,
Absorption Factor = A measure of the amount of chemical that crosses a biological boundary such as the skin and lungs (%), and

Body Weight = Body weight determined to represent the population of interest in a risk assessment (kg).

Margin of Exposure: Non-cancer risk estimates for each application handler scenario are calculated using a Margin of Exposure (MOE), which is a ratio of the toxicological endpoint to the daily dose of concern. The daily dermal and inhalation dose received by occupational handlers are compared to the appropriate POD (*i.e.* NOAEL) to assess the risk to occupational handlers for each exposure route. Only inhalation MOEs were calculated for short/intermediate term mancozeb exposures because no effects were observed in mancozeb 28 day dermal toxicity study, however, mancozeb daily dermal doses were calculated since they were used for the ETU risk estimate calculations.

All MOE values were calculated using the following formula:

$$MOE = \frac{POD \text{ (typically a NOAEL in mg/kg/day)}}{ADD \text{ (mg/kg/day)}}$$

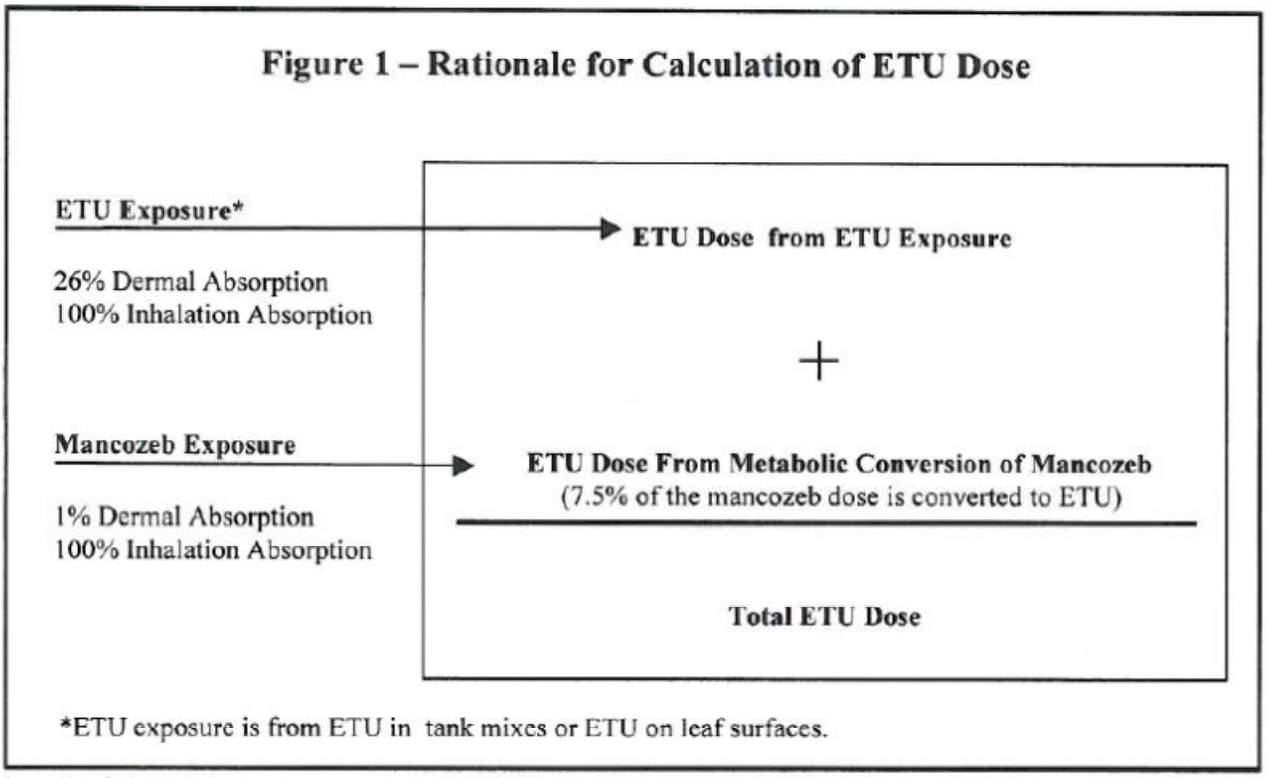
where:
MOE = Margin of Exposure: value used by HED to represent risk or risk estimates (unitless),
POD = Point of Departure,
NOAEL = No Observed Adverse Effect Level (mg/kg/day): Dose level in a toxicity study, where no observed adverse effects occurred in the study, and
ADD = Average Daily Dose (mg/kg/day): the absorbed dose received from exposure to a pesticide in a given scenario.

Risk calculations were also performed to assess the risk of ETU that is a degradate in the mancozeb spray mix and that is metabolized from absorbed mancozeb. The non-cancer risk calculations for exposures by occupational handlers to ETU were calculated in the same manner as for mancozeb with additional conversions that account for the absorption of ETU as well as the metabolic conversion of absorbed mancozeb into ETU. These calculations are described below:

Daily Exposure: The daily exposure was calculated from environmental sources of ETU (direct exposure via dermal or inhalation absorption) and from metabolic sources of ETU (mancozeb metabolically converted to ETU). Figure 1 provides a graphic illustration of this approach.

Sources of ETU exposure:
Environmental Sources of ETU (direct exposure via dermal or inhalation absorption)*:*
- ETU deposited on the skin during mixing/loading or application and then absorbed;
- ETU inhaled during mixing/loading or application and then absorbed;
-

Metabolic Sources of ETU (mancozeb metabolically converted to ETU)*:*
- Mancozeb deposited on the skin during mixing/loading or application, absorbed, then metabolically converted to ETU; and
- Mancozeb inhaled during mixing/loading or application, absorbed, then metabolically converted to ETU.



The following formulas were used for calculating dermal and inhalation exposures from ETU:

*Daily Exposure (mg ai /day) = UE (µg ai / lb ai) * AR (lb ai /A) * AT (A /day) * 1E-3 mg/µg* Tank Mix ETU (%)*

where:

Daily Exposure	=	Amount (mg ai/day) that is available for dermal or inhalation absorption (*i.e.*, ETU Daily Exposure from Tank Mixes During Mix/Loading/Applying)
UE	=	Unit Exposure (µg ai / lb ai).
AR	=	maximum application rate according to proposed label (lb ai /A), and
AT	=	daily acres treated (A /day).
Tank Mix ETU	=	level of ETU contamination in the tank mix that results from degradation of mancozeb. This level is 0.1 (for mixing and loading) or 0.2 (for application) percent of the parent.

The daily dose was calculated by normalizing the daily exposure value by body weight and accounting for dermal or inhalation absorption. A female body weight of 69 kg was used for short/intermediate term exposures because the POD is based on developmental and/or fetal effects while an average body weight of 80 kg was used for cancer risks because the chronic effects were not gender specific. The dermal absorption factors are 1 percent for mancozeb and 26 percent for ETU. The metabolic conversion factor of 7.5 percent mancozeb to ETU was used in all cases. Since no inhalation absorption data are available, toxicity by the inhalation route is considered to be equivalent to the estimated toxicity by the oral route of exposure (100%).

The daily doses were calculated for all sources of ETU exposure (*i. e.*, environmental and metabolic conversion of absorbed EBDC to ETU).

Daily doses for ETU exposures that occurred via direct contact with ETU (*i.e.*, environmental sources) were calculated using the following formula:

$$\textit{ETU Average Daily Dose from Direct Exposure to ETU (mg/kg/day)} = \frac{\textit{[Daily Exposure (mg ai/day) * Absorption (\%)]}}{\textit{Body Weight (kg)}}$$

where:

Average Daily Dose = Absorbed dose received from exposure to a pesticide in a given scenario *(i.e.,* ETU Average Daily Dose from Direct Exposure to ETU*);* (mg pesticide active ingredient/kg body weight/day),

Daily Exposure = Amount of ETU deposited on the surface of the skin that is available for dermal absorption or amount that is inhaled (mg ai/day);

Absorption Factor = A measure of the amount of chemical that crosses a biological boundary such as the skin and lungs (%).Dermal absorption factors are 26 percent for ETU; Inhalation absorption factors are 100 percent for ETU.

and

Body Weight = Body weight determined to represent the population of interest in a risk assessment (kg); 69 kg for short/intermediate term exposure, 80 for ETU cancer estimates.

Daily doses for ETU exposures resulting from metabolic conversion of absorbed mancozeb were calculated using the following formula:

$$\textit{ETU Average Daily Dose From metabolic conversion of mancozeb (mg/kg/day)} = \frac{\textit{[Daily Exposure (mg ai/day) * Absorption (\%)*Metabolic ETU Conversion]}}{\textit{Body Weight (kg)}}$$

where:

Average Daily Dose = Absorbed dose received from exposure to a pesticide in a given scenario *(i.e.,* ETU Average Daily Dose From metabolic conversion of mancozeb*);* (mg pesticide active ingredient/kg body weight/day),

Daily Exposure = Amount of mancozeb deposited on the surface of the skin (mg ai/day) that is available for dermal or inhalation absorption (from mancozeb potential exposure calculations),

Absorption Factor = A measure of the amount of chemical that crosses a biological boundary such as the skin and lungs (%).Dermal absorption factors are 1 percent for mancozeb. Inhalation absorption factors are 100 percent for both mancozeb and ETU. and

Metabolic ETU Conversion = 7.5 percent of the absorbed mancozeb dose is metabolically converted to ETU.

Body Weight = Body weight determined to represent the population of interest in a risk assessment (kg) 69 kg for short/intermediate term exposure, 80 for chronic exposures and ETU.

Dermal and inhalation absorbed average daily dose (ADD) values from both environmental and metabolic sources of ETU are then added together to obtain total daily dose values. These values also serve as the basis for the cancer risk estimates.

Margin of Exposure: Non-cancer risk estimates for each application handler scenario are calculated using a Margin of Exposure (MOE), which is a ratio of the toxicological endpoint to the daily dose of concern. The daily dermal and inhalation dose received by occupational handlers were compared to the appropriate POD (*i.e.* NOAEL) to assess the risk to occupational handlers for each exposure route. All MOE values were calculated using the following formula:

$$\textit{MOE} = \frac{\textit{POD (typically a NOAEL in mg/kg/day)}}{}$$

ADD (mg/kg/day)

where:
MOE = Margin of Exposure: value used by HED to represent risk or risk estimates (unitless),
POD = Point of Departure,
NOAEL = No Observed Adverse Effect Level (mg/kg/day): Dose level in a toxicity study, where no observed adverse effects occurred in the study, and
ADD = Average Daily Dose (mg/kg/day): the absorbed dose received from exposure to a pesticide in a given scenario.

As mentioned previously, only inhalation MOEs were calculated for mancozeb exposures because no effects were observed in the mancozeb 28-day dermal toxicity study. In the case of ETU, however, both inhalation and dermal exposures were considered for both non-cancer and cancer risk assessments. The level of concern (LOC) for mancozeb occupational risk assessments is for MOEs below 300 for females 13-49 years old, and 30 for males and females > 49 years old. The level of concern LOC for ETU occupational risk assessments is for MOEs below 1000. For ETU, dermal and inhalation risk estimates were combined in this assessment, since the toxicological effects for these exposure routes were similar. ETU dermal and inhalation risk estimates were combined using the following formula:

ETU Total MOE = Point of Departure (mg/kg/day) / Combined dermal + inhalation dose (mg/kg/day)

Summary of Occupational Handler Non-Cancer Exposure and Risk Estimates
HED has no data to assess exposures to pilots using open cockpits. The only data available is for exposure to pilots in enclosed cockpits. Therefore, risks to pilots are assessed using the engineering control (enclosed cockpits) and baseline attire (long-sleeve shirt, long pants, shoes, and socks); pilots are not required to wear protective gloves. With this level of protection, there are no risk estimates of concern for applicators.

All mixer/loader non-cancer risk scenarios do not exceed HED's level of concern (*i.e.*, MOEs ≥ 300 for mancozeb exposures and MOEs ≥1000 for ETU exposures), at some level of risk mitigation (*e.g.,* gloves, respirators, or other engineering control measures). Non-cancer risk estimates for M/L liquids in support of air and airblast applications ranged from MOE=10,500 (females 13-49 years old) to MOE=106,600 (males and females >49 years old) at label PPE (*i.e.,* gloves, no respirator). However, non-cancer risks estimates for M/L scenarios using dry flowable (DF) formulations in support of aerial applications exceed HED's level of concern (*i.e.,* MOE=260 for mancozeb inhalation exposures and MOE=750 for ETU exposures) at label PPE. It should be noted that no respiratory protection equipment or other engineering control measures are requested on the DF labels.

Likewise, all application non-cancer risk scenarios do not exceed HED's level of concern at some level of risk mitigation *(e.g.,* gloves or other engineering control measures). Aerial and airblast applicator risks do not exceed HED's level of concern (*i.e.*, MOEs ≥ 300 for mancozeb exposures and MOEs ≥1000 for ETU exposures) with engineering control (*i.e.,* enclosed cockpit or closed cab). Mixer/loader/ applicators with mechanically pressurized handgun risks do not exceed HED's level of concern at label PPE (*i.e.,* gloves, no respirator). The handler risks estimates (*i.e.,* non-

cancer) for mixing/loading (M/L) and application scenarios of the proposed mancozeb formulations on walnuts are presented on Tables 7 and 8.

Table 7. Short-/Intermediate-Term Occupational Non-Cancer Exposure and Risk Estimates for Mancozeb. All estimates are at baseline mitigation (*i.e.,* without respirator, unless specified).

Exposure Scenario [6]	Crop or Target	LOC	Inhalation Unit Exposure (ug/lb ai)[1]	Maximum Application Rate[2]	Area Treated or Amount Handled Daily[3]	Inhalation	
			Mitigation Level			Dose (mg/kg/day)[4]	MOE[5]
Mixer/Loader (Adult Males, Females >49 years)							
M/L, DF/WDG, Aerial, Broadcast	Walnuts	30	8.96	1.8 lb ai/acre	350 acres	0.070560	300
						0.014112 (PF5 Respirator)[7]	1,500
M/L, DF/WDG, Airblast, Broadcast					40 acres	0.008064	2,600
M/L, L/SC Aerial, Broadcast			0.219		350 acres	0.001725	12,200
M/L, L/SC Airblast, Broadcast					40 acres	0.000197	106,600
Mixer/Loader (Females 13-49 years)							
M/L, DF/WDG, Aerial, Broadcast	Walnuts	300	8.96	1.8 lb ai/acre	350 acres	0.081808	**260**
						0.016361 (PF5 Respirator)	1,300
M/L, DF/WDG, Airblast, Broadcast					40 acres	0.009349	2,200
M/L, L/SC, Aerial, Broadcast			0.219		350 acres	0.002000	10,500
M/L, L/SC; Airblast, Broadcast					40 acres	0.000228	92,000
Applicator (Adult Males, Females >49 years)							
Applicator, Spray, Aerial, Broadcast	Walnuts	30	0.068 (Engineering Control)	1.8 lb ai/acre	350 acres	0.000536	39,200
Applicator, Spray, Airblast, Broadcast (Open Cab)			4.71		40 acres	0.004239	5,000
Applicator, Spray, Airblast, Broadcast (Closed Cab)			0.068 (Engineering Control)		40 acres	0.000061	343,100
Applicator (Females 13-49 years)							
Applicator, Spray, Aerial, Broadcast	Walnuts	300	0.068 (Engineering Control)	1.8 lb ai/acre	350 acres	0.000621	33,800
Applicator, Spray, Airblast, Broadcast (Open Cab)			4.71		40 acres	0.004914	4,300
Applicator, Spray, Airblast, Broadcast			0.068		40 acres	0.000070	297,000

Table 7. Short-/Intermediate-Term Occupational Non-Cancer Exposure and Risk Estimates for Mancozeb. All estimates are at baseline mitigation (*i.e.,* without respirator, unless specified).

Exposure Scenario [6]	Crop or Target	LOC	Inhalation Unit Exposure (ug/lb ai)[1]	Maximum Application Rate[2]	Area Treated or Amount Handled Daily[3]	Inhalation	
			Mitigation Level			Dose (mg/kg/day)[4]	MOE[5]
(Closed Cab)			(Engineering Control)				
Mixer/Loader/Applicator (Adult Males, Females >49 years)							
M/L/A, DF/WDG, Mechanically-pressurized Handgun, Broadcast	Walnuts	30	3.9	0.018 lb ai/gallon	1000 gallons	0.000878	23,930
Mixer/Loader/Applicator (Females 13-49 years)							
M/L/A, L/DF/WDG, Mechanically-pressurized Handgun, Broadcast	Walnuts	300	3.9	0.018 lb ai/gallon	1000 gallons	0.001017	20,600

[1] Based on "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (**[**March 2012**]**); includes data from PHED/ORETF/AHETF (level of mitigation: Baseline, PPE, Eng. Controls).
[2] Based on registered labels (Reg. No. 70506-185**,** 70506-194**,** 70506-234**,** 70506-236).
[3] Exposure Science Advisory Council Policy #9.1.
[4] Inhalation Dose = Dermal Unit Exposure (ug/lb ai) x Conversion Factor (0.001 mg/ug) x Application Rate (lb ai/acre or gal) x Area Treated or Amount Handled Daily (A or gal/day) /BW (kg).
[5] Inhalation MOE = Inhalation NOAEL (mg/kg/day)/ Inhalation Dose (mg/kg/day).
[6] WDG- Water Dispersible Granules; DF- Dry Flowable; L/SC– Liquid/Soluble Concentrate
[7] PF5 Respirator is a respirator with a protection factor of 5 (*i.e.*, it provides 80 percent inhalation protection).

Table 8. Short-/Intermediate -Term Occupational Non-Cancer Exposure and Risk Estimates for ETU. All estimates are at label PPE (*i.e.*, gloves, no respirator, unless specified.

Exposure Scenario	Crop or Target	Dermal Unit Exposure (ug/lb ai)[1]	Inhalation Unit Exposure (ug/lb ai)[1]	Maximum Application Rate[2]	Area Treated or Amount Handled Daily[3]	ETU Dermal Dose (mg/kg/day)[6]		ETU Inhalation Dose (mg/kg/day)[6]		Total ETU Dose (mg/kg/day)[7]	Total MOE[8]
		Mitigation Level	Mitigation Level			ETU from Direct Exposure (Present in Tank Mix)[4]	ETU Metabolized from Mancozeb[5]	ETU from Direct Exposure (Present in Tank Mix)[4]	ETU Metabolized from Mancozeb[5]		
Mixer/Loader (Females 13-49 years)											
M/L, DF/WDG, Aerial, Broadcast	Walnuts	51.6	8.96	1.8 lb ai/acre	350 acres	0.000122	0.000353	0.000081	0.006135	0.006693	**750**
						0.000122	0.000353	0.000001 (PF5 Respirator)	0.001243 (PF5 Respirator)	0.001719 (PF5 Respirator)	2,900
M/L, DF/WDG, Airblast, Broadcast					40 acres	0.000014	0.000040	0.000009	0.000701	0.000764	6500
M/L, L/SC/EC, Aerial, Broadcast		37.6	0.219		350 acres	0.000089	0.000029	0.000002	0.000049	0.000498	10,000
M/L, L/SC/EC, Airblast, Broadcast					40 acres	0.000010	0.000029	0.000000	0.000017	0.000056	87,700
Applicator (Females 13-49 years)											
Applicator, Spray, Aerial, Broadcast	Walnuts	5.0 (Engineering Control)	0.068 (Engineering Control)	1.8 lb ai/acre	350 acres	0.000023	0.000034	0.000001	0.000046	0.000105	47,300
Applicator, Spray, Airblast, Broadcast (Open Cab)		1,590	4.71		40 acres	0.000863	0.001244	0.000009	0.000369	0.002486	2,000
Applicator, Spray, Airblast, Broadcast (Closed Cab)		14.6	0.068 (Engineering Control)		40 acres	0.000008	0.000011	0.0000001	0.000005	0.000025	202,000
Mixer/Loader/Applicator (Females 13-49 years)											
M/L/A, L/DF/WDG, Mechanically-pressurized Handgun, Broadcast	Walnuts	390	3.9	0.0180 lb ai/gallon	1000 gallons	0.000053	0.000076	0.000002	0.000076	0.000208	24,100

[1] PHED (level of mitigation: Baseline, PPE, Eng. Controls).
[2] Based on registered labels (Reg. No. 70506-185**,** 70506-194**,** 70506-234**,** 70506-236).
[3] Exposure Science Advisory Council Policy #9.1.

Daily Exposure = Unit Exposure (ug/lb ai) x Conversion Factor (0.001 mg/ug) x Application Rate (lb ai/acre or gal) x Area Treated or Amount Handled (A or gal/day) x DAF (%)

[4].ETU Average Daily Dose from Direct Exposure to ETU (mg/kg/day) = [Daily Exposure (mg ai/day) * Absorption (%)]/ BW (kg)
Absorption =0.1 (for mixing and loading) or 0.2 (for application) % of mancozeb.

[5] ETU Average Daily Dose From metabolic conversion of mancozeb (mg/kg/day) = [Daily Exposure (mg ai/day) * Absorption (%)*Metabolic ETU Conversion]/ BW (kg)
7.5 percent of the absorbed mancozeb dose is metabolically converted to ETU

[6] Dermal or Inhalation Dose= ETU Average Daily Dose from Direct Exposure to ETU (mg/kg/day) + ETU Average Daily Dose From metabolic conversion of mancozeb (mg/kg/day)

[7]Total ETU Dose = Total Dermal ETU Dose (mg/kg/day) + Total Inhalation ETU Dose (mg/kg/day)

[8]Total MOE = NOAEL (mg/kg/day)/Total ETU Dose (mg/kg/day). ETU Short/ Intermediate-Term Dermal and Inhalation NOAEL= 5 mg/kg/day. LOC=1000

Occupational Handler Cancer Exposure and Risk Equations

Cancer risk estimates were calculated using a linear low-dose extrapolation approach in which a Lifetime Average Daily Dose (LADD) is first calculated and then compared with a Q_1^* that has been calculated for ETU based on dose response data in the appropriate toxicology study ($Q_1^* = 6.01 \times 10^{-2}$ (mg/kg/day)$^{-1}$). Absorbed average daily dose (ADD) levels were used as the basis for calculating the LADD values. Dermal and inhalation ADD values were first added together to obtain combined ADD values. LADD values were then calculated and compared to the Q_1^* to obtain cancer risk estimates.

Lifetime Average Daily Dose: After the development of the ADD values, the next step required to calculate the carcinogenic risk estimate is to amortize these values over the working lifetime of occupational handlers based on use patterns, which results in the LADD for that use. Product labels limit use to 10 applications per year. Based on this information and due to the number and variety of target diseases and crops registered for EBDC applications, the Agency considered two distinct populations in the cancer risk assessment including private applicators at 10 use events per year and commercial applicators that would have a more frequent use pattern of 30 days per year. Finally, a 35 year career and a 78 year lifespan were used to complete the calculations. LADD values were calculated using the following equation:

$$LADD = ADD \times \frac{\text{Days per year of exposure}}{\text{365 days/year}} \times \frac{\text{Years per Lifetime of exposure}}{\text{Lifetime Expectancy}}$$

where:

LADD	=	Lifetime Average Daily Dose- the amount as absorbed dose received from exposure to a pesticide in a given scenario over a lifetime (mg pesticide active ingredient/kg body weight/day),
ADD	=	Average Daily Dose- the amount as absorbed dose received from exposure to a pesticide in a given scenario on a daily basis (mg pesticide active ingredient/kg body weight/day),
Days per year of exposure	=	the annual frequency of an application by an individual (days/year),
Years per Lifetime of exposure	=	the amount of a lifetime that an individual spends engaged in a career involving pesticide exposure (35 years), and
Lifetime Expectancy	=	the average life expectancy of an individual (78 years).

Cancer Risk Estimates: Finally, cancer risk estimate calculations were completed by comparing the LADD values calculated above to the Q_1^* for ETU ($Q_1^* = 6.01 \times 10^{-2}$ (mg/kg/day)$^{-1}$). The Agency considered more typical users in these calculations (*i.e.*, private applicators at 10 events per year) as well as more frequent users that might represent commercial applicators (*i.e.*, 30 events per year). Cancer risk estimates were calculated using the following equation:

$$\text{Total Cancer Risk Estimate} = (\text{Dermal LADD} + \text{Inhalation LADD}) \times Q_1^*$$

where:

Cancer Risk Estimate	=	Probability of incidence of cancer cases over a lifetime (unitless),
Dermal LADD	=	Dermal Lifetime Average Daily- Dose the amount as absorbed dose received from dermal exposure to a pesticide in a given scenario over a lifetime (mg pesticide active ingredient/kg body weight/day),
Inhalation LADD	=	Inhalation Lifetime Average Daily Dose- the amount as absorbed dose received

		from inhalation exposure to a pesticide in a given scenario over a lifetime (mg pesticide active ingredient/kg body weight/day), and
Q_1*	=	Quantitative dose response factor used for linear, low-dose response cancer risk calculations $(mg/kg/day)^{-1}$.

Summary of Occupational Handler Cancer Exposure and Risk Estimates

The cancer risks for all mixing/loading (M/L) scenarios for private handlers are estimated in the 10^{-6} to 10^{-8} range at label PPE (*i.e.,* gloves, no respirator). Cancer risks for both private and commercial handlers M/L liquids in support of air and airblast applications ranged from 9.5×10^{-7} to 3.6×10^{-8} at label PPE. Cancer risks for commercial handlers M/L scenarios using dry flowable (DF) formulations in support of aerial applications ranged from 1.3×10^{-5} at label specified PPE, to 4.9×10^{-7} with the use of water soluble bags (WSB) as an engineering control measure. Cancer risks for commercial handlers M/L scenarios using DF formulations in support of airblast applications ranged from 1.5×10^{-6} at label PPE, to 3.8×10^{-7} with additional PPE (*i.e.,* PF5 respirator). Cancer risks for private handlers mixing/loading DF formulations in support of aerial applications ranged from 4.3×10^{-6} at label PPE, to 7.0×10^{-7} with additional PPE (*i.e.,* PF10 respirator). Cancer risks for private handlers mixing/loading DF formulations in support of airblast applications were estimated at 4.9×10^{-7} at label PPE.

The cancer risks for all application scenarios are estimated in the 10^{-6} (open cab airblast applications) to 10^{-8} range for both private and commercial handlers (closed cab or cockpit for airblast and aerial applications, respectively) The cancer risks for mixing/loading/application (M/L/A) scenarios are estimated in the 10^{-7} range for both private and commercial handlers at label PPE.

HED has no level of concern/target for presenting cancer risk estimates. The cancer risk estimates are presented based on the Q_1* value for OPP risk managers to evaluate and mitigate as needed. A summary of occupational handler cancer risks for applying mancozeb for the proposed uses is presented on Table 9.

Table 9. Short/Intermediate-term Occupational Cancer Exposure and Risk Estimates for ETU from Mancozeb.
All estimates are at label PPE (*i.e.* gloves, no respirator) unless specified.

Crop or Target	Exposure Scenario	Handler Dermal ADD[1] (mg/kg/day)	Handler Inhalation ADD[2] (mg/kg/day)	Total LADD[c]		Cancer			
				Private Handler	Commercial Handler	Private Handler		Commercial Handler	
				LADD[3] (mg/kg/day)	LADD (mg/kg/day)[3]	Mitigation Level	Risk Estimate[4]	Mitigation Level	Risk Estimate[4]
Mixer/Loader									
Walnuts	M/L, DF/WDG, Aerial, Broadcast	0.000476	0.006217	7.09×10^{-5}	2.13×10^{-4}	Gloves	4.3×10^{-6}	Gloves	1.3×10^{-5}
		0.000476	0.001243	1.82×10^{-5}	5.47×10^{-5}	Gloves, PF 5 R[5]	1.1×10^{-6}	Gloves, PF 5 R[5]	3.3×10^{-6}
		0.000476	0.000622	1.16×10^{-5}	3.49×10^{-5}	Gloves, PF 10 R	7.0×10^{-7}	Gloves, PF 10 R	2.1×10^{-6}
		0.000090	0.000167	NA	8.17×10^{-6}	WSB[6] (Engineering Control)	NA	WSB[6] (Engineering Control)	4.9×10^{-7}
	M/L, DF/WDG, Airblast, Broadcast	0.000054	0.000711	8.11×10^{-6}	2.43×10^{-5}	Gloves	4.9×10^{-7}	Gloves	1.5×10^{-6}
		0.000054	0.000142	NA	6.25×10^{-6}	Gloves, PF 5 R[5]	NA	Gloves, PF 5 R[5]	3.8×10^{-7}
	M/L, L/SC/EC, Aerial, Broadcast	0.000347	0.000152	5.28×10^{-6}	1.59×10^{-5}	Gloves	3.2×10^{-7}	Gloves	9.5×10^{-7}
	M/L, L/SC/EC, Airblast, Broadcast	0.000040	0.000017	1.04×10^{-7}	1.81×10^{-6}	Gloves	3.6×10^{-8}	Gloves	1.1×10^{-7}
Applicator									
Walnuts	Applicator, Spray, Aerial, Broadcast	0.000058	0.000048	$1,12 \times 10^{-6}$	3.37×10^{-6}	Closed Cockpit	6.5×10^{-8}	Closed Cockpit	2.0×10^{-7}
	Applicator, Spray, Airblast, Broadcast (Open Cab)	0.002107	0.000378	2.63×10^{-5}	7.91×10^{-5}	Open Cab/No respirator	1.6×10^{-6}	Open Cab/No respirator	4.8×10^{-6}
		0.000019	0.000076	2.31×10^{-5}	6.94×10^{-5}	Open Cab/ PF 5 R	1.4×10^{-6}	Open Cab/ PF 5 R	4.2×10^{-6}
	Applicator, Spray, Airblast, Broadcast	0.000019	0.000005	2.63×10^{-7}	7.89×10^{-7}	Closed Cab	1.6×10^{-8}	Closed Cab	4.7×10^{-8}

Table 9. Short/Intermediate-term Occupational Cancer Exposure and Risk Estimates for ETU from Mancozeb.
All estimates are at label PPE (*i.e.* gloves, no respirator) unless specified.

Crop or Target	Exposure Scenario	Handler Dermal ADD[1] (mg/kg/day)	Handler Inhalation ADD[2] (mg/kg/day)	Total LADD[c]		Cancer			
				Private Handler	Commercial Handler	Private Handler		Commercial Handler	
				LADD[3] (mg/kg/day)	LADD (mg/kg/day) [3]	Mitigation Level	Risk Estimate[4]	Mitigation Level	Risk Estimate[4]
	(Closed Cab)								
Mixer/Loader/Applicator									
Walnuts	M/L/A, L/DF/WDG, Mechanically-pressurized Handgun, Broadcast	0.000129	0.000078	2.2×10^{-6}	6.6×10^{-6}	Gloves	1.3×10^{-7}	Gloves	4.0×10^{-7}

[1] Dermal ADD = Dermal Absorbed Daily Dose
[2] Inhalation ADD = Inhalation Absorbed Daily Dose
[3] Total LADD = total absorbed dose [Dermal dose + Inhalation Dose] * Days per year of exposure * Years per lifetime of exposure / (365 days/year x Lifetime expectancy).
[4] Cancer risk estimates = LADD * Q_1^*, where $Q_1^* = 6.01 \times 10^{-2}$ $(mg/kg/day)^{-1}$.
[5]. PF5 Respirator**:** is a respirator with a protection factor of 5
[6]. WSB Water soluble bags (engineering control)

5.2 Occupational Post-application Exposures/Risks Estimates

HED uses the term post-application to describe exposures that occur when individuals are present in an environment that has been previously treated with a pesticide (also referred to as re-entry exposure). Such exposures may occur when workers enter previously treated areas to perform job functions, including activities related to crop production, such as scouting for pests or harvesting. Post-application exposure levels vary over time and depend on such things as the type of activity, the nature of the crop or target that was treated, the type of pesticide application, and the chemical's degradation properties. In addition, the timing of pesticide applications, relative to harvest activities, can greatly reduce the potential for post-application exposure.

Occupational re-entry workers may experience short-/intermediate-term exposure to mancozeb while performing post-application activities. ETU can also be found as an environmental degradate in post-application monitoring studies on agricultural crops and turf so the Agency has also evaluated direct exposures to post-application workers as appropriate. Finally, ETU can be formed in the human body via various metabolic pathways after mancozeb is absorbed. The contributions of this metabolic conversion are also considered in the assessment for ETU. The studies presented in this section monitored for both mancozeb residues and ETU residues.

5.2.1 Occupational Post-application Inhalation Exposure/Risk Estimates

Based on the Agency's current practices, a quantitative post-application inhalation exposure assessment was not performed for mancozeb or for its degradate, ETU, at this time primarily because of the low acute inhalation toxicity (Toxicity Category IV). However, there are multiple potential sources of post-application inhalation exposure to individuals performing post-application activities in previously treated fields. These potential sources include volatilization of pesticides and resuspension of dusts and/or particulates that contain pesticides. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009, and received the SAP's final report on March 2, 2010[8]. The Agency is in the process of evaluating the SAP report as well as available post-application inhalation exposure data generated by the ARTF and may, as appropriate, develop policies and procedures, to identify the need for and, subsequently, the way to incorporate occupational post-application inhalation exposure into the Agency's risk assessments. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative occupational post-application inhalation exposure assessment for mancozeb.

Although a quantitative occupational post-application inhalation exposure assessment was not performed, an inhalation exposure assessment was performed for occupational/commercial handlers. Handler exposure resulting from application of pesticides outdoors is likely to result in higher exposure than post-application exposure. The airblast application handler scenario[9] is believed to represent a reasonable worst-case surrogate estimate of post-application inhalation

[8] Available: http://www.epa.gov/scipoly/SAP/meetings/2009/120109meeting.html

[9] See Tables 7,8, and 9 for a description of non-cancer and cancer risk estimates for commercial and private grower applications of mancozeb on walnut crops.

exposure during typical post-application activities on nut crops (*e.g.*, mechanical harvesting activities). The use of the handler scenario of airblast application for translation to the inhalation exposure of harvesting is a very conservative assumption. It is assuming harvesting inhalation exposure to be the same as on the last day of treatment. Furthermore, it should be noted that the labels specify a pre-harvest interval of 75 days. Hence, some dissipation of mancozeb residue can be assumed to occur by the harvesting day through chemical degradation or environmental dissipation. Therefore, it is expected that these handler inhalation exposure estimates would be protective of most occupational post-application inhalation exposure scenarios.

5.2.2 Occupational Post-application Dermal Exposure/Risk Estimates

Occupational Post-application Dermal Exposure Data and Assumptions

Since there is no dermal endpoint identified for mancozeb, only dermal post-application assessment for its degradate ETU has been conducted. A series of assumptions and exposure factors served as the basis for completing the occupational post-application risk assessments. Each assumption and factor is detailed below on an individual basis.

Exposure Duration:
Occupational re-entry workers may experience short-/intermediate-term exposure to mancozeb and ETU residues while performing post-application activities. To assess cancer risk, it is assumed that private growers would be exposed 10 days per year and commercial applicators would be exposed 30 days per year. The term "private grower" means that the grower or one of the workers would apply the pesticides to land owned or operated by the grower. "Commercial applicators" are assumed to complete multiple applications for multiple clients.

Transfer Coefficients:
It is the policy of HED to use the best available data to assess post-application exposure. Sources of generic post-application data, used as surrogate data in the absence of chemical-specific data, are derived from ARTF exposure monitoring studies, and, as proprietary data, are subject to the data protection provisions of FIFRA. The standard values recommended for use in predicting post-application exposure that are used in this assessment, known as "transfer coefficients", are presented in the ExpoSAC Policy 3[10]" which, along with additional information about the ARTF data, can be found at the Agency website[11]. A summary of anticipated post-applications activities for the proposed use on walnuts is presented on Table 10.

Table 10. Anticipated Post-Application Activities and Dermal Transfer Coefficients.

Proposed Crops	Policy Crop Group Category	Crop Height	Foliage Density	Transfer Coefficients cm^2/hr	Activities
Walnuts	Group 14 (Tree, nut)	High	Full	100	Orchard maintenance
		High	Full	580	Scouting
		High	Full	100	Weeding, Hand
		Low	Min	230	Transplanting

10 Available: http://www.epa.gov/pesticides/science/exposac_policy3.pdf
11 Available: http://www.epa.gov/pesticides/science/post-app-exposure-data.html

Table 10. Anticipated Post-Application Activities and Dermal Transfer Coefficients.					
Proposed Crops	Policy Crop Group Category	Crop Height	Foliage Density	Transfer Coefficients cm^2/hr	Activities
		High	Full	190	Harvesting (mechanical shaking)

Application Rate:
A single maximum application rate of 1.8 lb ai/acre is the basis for this assessment. The labels propose a maximum of ten applications per year (*i.e.,* maximum total application rate of 18 lb ai/year), and a Pre-Harvest Interval (PHI) of 75 days. Applications are to begin at early pre-bloom prior to or when catkins are partially expanded and additional applications can be made during bloom and early nutlet stage, or as needed if frequent rainfall occurs.

Body Weight:
- A body weight of 69 kg was used for assessing ETU non-cancer risks since the dermal POD is based on developmental and/or fetal effects.
- The standard body weight for the general population (80 kg) was used for assessing ETU cancer risks since the endpoints selected were not developmental and/or fetal effects.

Absorption factor:
A dermal absorption factor of 1 % was used for mancozeb. A dermal absorption factor of 26 % was used for ETU. A metabolic conversion factor of 7.5 % [12] of the absorbed mancozeb dose is used to calculate the ETU dose due to in-vivo metabolism.

Exposure Time:
The average occupational workday is assumed to be 8 hours.

Dislodgeable Foliar Residues:
Eight dislodgeable foliar residue (DFR) studies were submitted in support of reregistration of mancozeb and these were reviewed in Mancozeb ORE Assessment for the RED (D317368, T. Dole, 05/31/05). The DFR studies were conducted on apples, grapes, and tomatoes using airblast and groundboom application of Dithane DF dry flowable fungicide. The DFR study selected for estimating post-application exposure on walnuts crops is shown in Table 11.

Table 11. Mancozeb/ETU DFR Study Data Used						
Crop Group (Labeled Crops)	Region	Study Used (MRID)[1]	Study Application Rate (lb ai/acre)	Parameters Matched	Initial DFR (ug/cm^2)	
					Mancozeb	ETU
Trees, Nut, (Walnuts)	West	WA Airblast Apple (449596-02)	1.8	Application method, climate	16.5	.053

[1]This study was previously used for evaluating post-application exposures on almonds (D391948, Rivera-Lupiáñez, A., 11/15/11 and D327307 & D327318, D. Davis, *et al*, 6/11/07).

[12] A. Kocialski, 09/12/1989. Memo: *Establishment of an in-vivo Metabolic Conversion Factor of 7.5%for all Ethylene Bis(Dithio) Carbamates (EBDCS)when Converting EBDCSs to Ethylene Thiourea (ETU) in- vivo.*

Days per year of exposure:
Product labels limit use to 10 applications per year. Based on this information and due to the number and variety of target diseases and crops registered for EBDC applications, the Agency considered two distinct populations in the cancer risk assessment including private applicators at 10 use events per year and commercial applicators that would have a more frequent use pattern of 30 days per year.

Years per Lifetime of Exposure:
HED assumes that post-application workers would be exposed for 35 years out of a 78 year lifespan.

Lifetime Expectancy:
Based on available data from EPA's Exposure Factors Handbook 2011 Edition, the recommended lifespan for use in cancer risk assessments is 78 years. Life expectancy values are derived from the Exposure Factors Handbook 2011 Edition Table 18-1 (U.S. EPA, 2011). The table shows that the overall life expectancy is 78 years based on life expectancy data from 2007. In 2007, the average life expectancy for males was 75 years and 80 years for females.

Occupational Post-application Non-Cancer Dermal Exposure and Risk Estimate Equations

Average Daily Dose (ADD): Potential daily exposures for occupational post-application workers were calculated using the following formulas:

$$DFR_t\ (\mu g/cm^2) = AR\ (lb\ ai/A) * F * (1\text{-}D)^t * 4.54E8\ \mu g/lb * 2.47E\text{-}8\ acre/cm^2$$

where:

DFR_t	=	dislodgeable foliage residue on day "t" ($\mu g/cm^2$),
AR	=	Application Rate (lb ai/acre)
F	=	fraction of ai retained on foliage or 25% (unitless)
D	=	fraction of residue that dissipates daily or 10% (unitless)
t	=	number of days after application day (days)

$$Daily\ Exposure\ (mg\ ai\ /day) = TC\ (cm^2/hr) * DFR_t\ (\mu g/cm^2) * ET\ (hrs\ /day) * 1E\text{-}3\ mg/\mu g$$

where:

Daily Exposure	=	Amount (mg ai/day) that is available for dermal absorption,
TC	=	Transfer coefficient (cm^2/hr),
DFR_t	=	Dislodgeable Foliar Residue on day "t" ($\mu g/cm^2$), and
ET	=	Exposure Time (hours /day).

The daily doses were calculated using the following formula:

$$Average\ Daily\ Dose\ (mg\ ai/kg/day) = \frac{[Daily\ Exposure\ (mg\ ai/day) * Absorption\ (\%)]}{Body\ Weight\ (kg)}$$

where:

Average Daily Dose	=	Absorbed dose received from exposure to a pesticide in a given scenario (mg pesticide active ingredient/kg body weight/day),
Daily Exposure	=	Amount (mg ai/day) that is available for dermal absorption,
Absorption Factor	=	A measure of the amount of chemical that crosses a biological boundary such as the skin (%), and

Body Weight = Body weight determined to represent the population of interest in a risk assessment (kg).

Margin of Exposure: Non-cancer risk estimates for each application handler scenario are calculated using a Margin of Exposure (MOE), which is a ratio of the toxicological endpoint to the daily dose of concern. The daily dermal dose received by occupational post-application workers was compared to the appropriate POD (*i.e.* NOAEL) to assess the risk to occupational post-application workers. Since there is no dermal endpoint identified for mancozeb, only dermal post-application assessment for its degradate ETU has been conducted. All MOE values were calculated using the following formula:

$$MOE = \frac{POD \text{ (typically a NOAEL in mg/kg/day)}}{ADD \text{ (mg/kg/day)}}$$

where:
MOE = Margin of Exposure: value used by HED to represent risk or risk estimates (unitless),
POD = Point of Departure,
NOAEL = No Observed Adverse Effect Level (mg/kg/day): Dose level in a toxicity study, where no observed adverse effects occurred in the study, and
ADD = Average Daily Dose (mg/kg/day): the absorbed dose received from exposure to a pesticide in a given scenario.

Occupational Post-application Non-Cancer Dermal Risk Estimates

Since there is no dermal endpoint identified for mancozeb, only dermal post-application assessment for its degradate ETU has been conducted. The level of concern for the ETU post-application occupational risk assessment is for MOEs below 1000. The ETU exposure was calculated by adding the ETU dose absorbed from the leaf surface (direct contact) to the ETU that is metabolically converted from absorbed mancozeb. These values also serve as the basis for the cancer risk estimates

All post-application occupational exposure scenarios assessed resulted in MOEs that do not exceed HED's level of concern (*i.e.*, ETU MOEs ≥ 1000) at mancozeb current Restricted Entry Interval (REI) of 24 hours which is also proposed for walnut crops. Post-application occupational non-cancer risks estimates are summarized in Table 12.

Table 12: Summary of Occupational/Commercial Post-application Non-Cancer Risk Estimates for ETU from Mancozeb [1]

Crop/Site	Activities	Transfer Coefficient (cm^2/hr)	ETU Foliar Dose [2] (mg/kg/day)	Mancozeb Metabolized Dose to ETU [3] (mg/kg/day)	Total Dermal Dose [4] (mg/kg/day)	MOE[5]
Short-term /Intermediate-term						
Walnuts	Orchard maintenance	100	0.000056	0.000050	0.000106	47,000
	Scouting	580	0.000325	0.000290	0.000611	8,100
	Weeding, Hand	100	0.000056	0.000050	0.000106	47,000
	Transplanting	230	0.000129	0.000115	0.000244	20,500
	Harvesting (mechanical shaking)	190	0.000107	0.000095	0.000202	24,800

1. Based on Mancozeb initial DFR of 16.5(ug/cm^2) and ETU initial DFR of 0.053 (ug/cm^2). Values from MRID 449596-02 (WA Airblast Apple)
2. ETU Foliar Dermal Dose = [DFR (µg/cm^2) × Transfer Coefficient × 0.001 mg/µg × 8 hrs/day × dermal absorption (%)] ÷ BW (kg).
3. Mancozeb Dermal Dose = [DFR (µg/cm^2) × Transfer Coefficient × 0.001 mg/µg × 8 hrs/day × dermal absorption (%)] ÷ BW (kg)
   ETU Metabolized Dose to ETU= Mancozeb Dermal Dose × 0.075
4. Total Dermal Dose = ETU Foliar Dermal Dose + ETU Metabolized Dose to ETU
5. MOE = POD (mg/kg/day) / Daily Dermal Dose. LOC= 1000

Restricted Entry Interval

Mancozeb is classified as Toxicity Category IV via the dermal route and Toxicity Category IV for skin irritation potential. Mancozeb is not a skin sensitizer. Mancozeb's degradate; ETU is not acutely toxic via the dermal or inhalation routes of exposure. ETU is not a skin or eye irritant. The interim 24-hour restricted re-entry interval (REI) on the proposed label is in compliance with the Worker Protection Standard (WPS) for agricultural pesticides and is consistent with previously approved REIs for registered formulations of mancozeb. Short- and intermediate-term post-application risk estimates were not a concern on day 1 (24 hours following application) for all post-application activities.

Occupational Post-application Cancer Dermal Exposure and Risk Equations

Cancer risks were assessed for all post-application activities on walnuts. As was done for occupational handlers, post-application cancer risk estimates were calculated using a linear low-dose extrapolation approach in which a Lifetime Average Daily Dose (LADD) is first calculated and then compared with a Q_1* that has been calculated for mancozeb's degradate, ETU, based on dose response data in the appropriate toxicology study (Q_1* = 6.01 x 10 $^{-2}$ (mg/kg/day)$^{-1}$). Absorbed average daily dose (ADD) levels were used as the basis for calculating the LADD values. After the development of the ADD values, the next step required to calculate the carcinogenic risk is to amortize these values over the working lifetime of the occupational workers with post-application exposure based on use pattern, which results in the LADD for that use. Product labels limit use to 10 applications per year. Based on this information and due to the number and variety of target diseases and crops registered for EBDC applications, the Agency considered two distinct populations in the cancer risk assessment including private applicators at 10 use events per year and commercial applicators that would have a more frequent use pattern of 30 days per year. A 35 year career and a 78 year lifespan were used to complete the calculations.

LADD values were calculated using the following equation:

$$LADD = ADD \times \frac{\text{Days per year of exposure}}{365 \text{ days/year}} \times \frac{\text{Years per lifetime of exposure}}{\text{Lifetime Expectancy}}$$

where:

LADD	=	Lifetime Average Daily Dose- the amount as absorbed dose received from exposure to a pesticide in a given scenario over a lifetime (mg pesticide active ingredient/kg body weight/day),
ADD	=	Average Daily Dose- the amount as absorbed dose received from exposure to a pesticide in a given scenario on a daily basis (mg pesticide active ingredient/kg body weight/day),
Days per year of exposure	=	the annual frequency of exposure by an individual (days/year),
Years per lifetime of exposure	=	the amount of a lifetime that an individual spends engaged in a career involving pesticide exposure (35 years), and
Lifetime Expectancy	=	the average life expectancy of an individual (78 years).

Cancer Risk Estimates: Finally, cancer risk estimate calculations were completed by comparing the LADD values calculated above to the Q_1^* for ETU ($Q_1^* = 6.01 \times 10^{-2}$ (mg/kg/day)$^{-1}$). Cancer risk estimates were calculated using the following equation:

*Cancer Risk Estimate = Dermal LADD (mg/kg/day) * Q_1^* (mg/kg/day)$^{-1}$*

where:

Cancer Risk Estimate	=	Probability of incidence of cancer cases over a lifetime (unitless),
Dermal LADD	=	Dermal Lifetime Average Daily Dose- The amount as absorbed dose received from dermal exposure to a pesticide in a given scenario over a lifetime (mg pesticide active ingredient/kg body weight/day, also referred to as LADD), and
Q_1^* risk		= Quantitative dose response factor used for linear, low dose response cancer calculations (mg/kg/day)$^{-1}$.

Occupational Post-application Cancer Dermal Risk Estimates

Since there is no dermal endpoint identified for mancozeb, only dermal post-application cancer risks estimates for its degradate ETU has been conducted. The ETU exposure was calculated by adding the ETU dose absorbed from the leaf surface (direct contact) to the ETU that is metabolically converted from absorbed mancozeb. These values also serve as the basis for the cancer risk estimates. The cancer risks for post-application scenarios assessed are in the 10^{-7} to 10^{-8} range for private growers and 10^{-6} to 10^{-7} for commercial growers at Day 1 (*i.e.,* at the 24 hour REI). Post-application occupational cancer risks estimates are summarized in Table 13.

Table 13. Occupational Post-Application Cancer Exposures and Risk Estimates for ETU from Mancozeb

Crop Grouping/Crop	Activity	Days After Treatment	Dermal LADD (mg/kg/day)[1]		Cancer Risk Estimate[2]	
			Private Grower	Commercial Grower	Private Grower	Commercial Grower
Trees, Nut, Crop Group 14 (Walnuts)	Orchard maintenance	1	0.00000112	0.00000337	6.8×10^{-8}	2.0×10^{-7}
	Scouting	1	0.00000652	0.00001957	3.9×10^{-7}	1.2×10^{-6}
		6	0.00000567	0.00001700	3.4×10^{-7}	1.0×10^{-6}
	Weeding, Hand	1	0.00000112	0.00000337	6.8×10^{-8}	2.0×10^{-7}
	Transplanting	1	0.00000258	0.00000776	1.6×10^{-7}	4.7×10^{-7}
	Harvesting (mechanical shaking)	1	0.00000213	0.00000641	1.3×10^{-7}	3.9×10^{-7}

[1] Dermal LADD = Dermal dose * Day per year of exposure x Years per lifetime of exposure / (365 days/year x Lifetime expectancy).

[2] Cancer risk estimates = LADD * Q_1^*, where $Q_1^* = 6.01 \times 10^{-2}$ (mg/kg/day)$^{-1}$

6.0 RESIDENTIAL (NON-OCCUPATIONAL) EXPOSURE AND RISK ESTIMATES

There are no proposed residential uses at this time; however, two residential uses that could result in mancozeb and ETU exposure (*i.e.,* home gardeners applying mancozeb to vegetables and golfers contacting mancozeb treated turf after application), have been reassessed in this document to reflect updates to toxicology endpoint selections, HED's 2012 Residential SOPs (http://www.epa.gov/pesticides/science/residential-exposure-sop.html), along with policy changes for body weight assumptions. The revision of residential exposures will impact the human health aggregate risk assessment for mancozeb.

The cancer risk to home gardeners and golfers were also reassessed in this document, as they will be used for the aggregate risk assessment. A summary of the exposure and risk associated with the registered residential uses is provided for use in performing an aggregate exposure and risk assessment.

6.1 Residential Handler Exposure/Risk Estimates

HED uses the term "handlers" to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct tasks related to applications and that exposures can vary depending on the specifics of each task as was described above for occupational handlers. Residential handlers are addressed somewhat differently by HED as homeowners are assumed to complete all elements of an application without use of any protective equipment.

Residential risks from mancozeb exposures have been assessed previously (D327307 & D327318; D. Davis, *et al.*, 6/11/07). A summary of the exposure and risk associated with the registered residential uses is provided for use in performing an aggregate exposure and risk assessment. The existing residential handler scenario identified for mancozeb is for the application of mancozeb in home gardens (*i.e.,* vegetables). HED notes that there are no direct homeowner applications of mancozeb to turf; however, there is a registered sod farm use and the treated sod could be subsequently transplanted to a residential setting. HED considers post-application exposure resulting from this scenario to be negligible for the following reasons: 1) mancozeb has a post-harvest interval (PHI) of 5 days for sod; 2) it is unlikely that sod treated with mancozeb would be installed more than once per year; 3) transplanted sod requires constant and significant watering which will result in decreased mancozeb residues on the transplanted sod; and 4) it is unlikely that adults or children will spend any significant amount of time on recently transplanted sod until it is rooted which typically occurs around 2 weeks after transplanting. Therefore, dermal and incidental oral post-application scenarios were not assessed for the sod farm use of mancozeb. The quantitative exposure/risk assessment developed for residential handlers is based on the following scenarios:

1. Adults Mixing/Loading/Applying liquids by Manually-pressurized handwand;
2. Adults Mixing/Loading/Applying liquids by Hose-End Sprayer; and
3. Adults Mixing/Loading/Applying liquids by Backpack.

Residential Handler Exposure Data and Assumptions

Only inhalation MOEs were calculated for short term mancozeb exposures because no effects were observed in mancozeb 28 day dermal toxicity study. Risk calculations were also performed to assess the risk of mancozeb's degradate ETU.

The non-cancer risk calculations for exposures by residential handlers to ETU were calculated in the same manner as for mancozeb with additional conversions that account for the absorption of ETU as well as the metabolic conversion of absorbed mancozeb into ETU. The daily exposure was calculated from environmental sources of ETU (direct exposure via dermal or inhalation absorption) and from metabolic sources of ETU (mancozeb metabolically converted to ETU).

A series of assumptions and exposure factors served as the basis for completing the residential handler risk assessments. Each assumption and factor is detailed below.

Application Rate:
According to registered labels a mancozeb formulation product (*i.e.*, Dithane F-45; EPA Reg. 62719-396) can be applied to home garden vegetables at a maximum single application rate of 2.4 lb ai/acre. Tank mix stability studies submitted to, and reviewed by, the Agency in 1991 indicated that 0.1 percent of the mancozeb parent converted to ETU during mixing/loading and 0.2 percent converted to ETU during application (D327307 & D327318; D. Davis, 6/11/07).

Unit Exposures and Area Treated or Amount Handled: Unit exposure values and estimates for area treated or amount handled were taken from HED's 2012 Residential SOPs (http://www.epa.gov/pesticides/science/residential-exposure-sop.html).

Body Weight

- The standard body weight for the general population (80 kg) was used for assessing mancozeb inhalation non-cancer risks and ETU cancer risks since the endpoints selected were not developmental and/or fetal effects.
- A body weight of 69 kg was used for assessing ETU non-cancer risks since the POD are based on developmental and/or fetal effects.
- Risk estimate results for both population sub-groups *(i.e.*, females 13 to 49 years old, and males and females>49 years old) are presented since the LOCs for these lifestage population groups are different.

Absorption Factors
A dermal absorption factor of 1 % was used for mancozeb. A dermal absorption factor of 26 % was used for ETU. A metabolic conversion factor of 7.5 % [13] of the absorbed mancozeb dose is used to calculate the ETU dose due to in-vivo metabolism. Since no inhalation absorption data are available, toxicity by the inhalation route is considered to be equivalent to the estimated toxicity by the oral route of exposure (100%).

Exposure Duration:
Residential handler exposure is expected to be short-term in duration. Intermediate-term exposures are not likely because of the intermittent nature of applications by homeowners.

[13] A. Kocialski, 09/12/1989. Memo: *Establishment of an in-vivo Metabolic Conversion Factor of 7.5%for all Ethylene Bis(Dithio) Carbamates (EBDCS)when Converting EBDCSs to Ethylene Thiourea (ETU) in- vivo.*

Residential Handler Non-Cancer Exposure and Risk Estimate Equations

The non-cancer risk calculations for exposures by residential handlers were calculated in a similar manner as for occupational handlers. The algorithms used to estimate exposure and dose for residential handlers can be found in the 2012 Residential SOPs (http://www.epa.gov/pesticides/science/residential-exposure-sop.html) and in Appendix A of this document.

Summary of Residential Handler Non-Cancer Exposure and Risk Estimates for Mancozeb

Residential handler inhalation risk estimates are not of concern (MOEs > LOC). Inhalation MOEs for mixing/loading/applying liquid formulation to vegetable gardens scenarios range from 170,000 for backpack sprayer applications to 20 million for hose-end sprayer applications. A summary of inhalation risk estimates for residential handlers can be found in Table 14.

Summary of Residential Handler Non-Cancer Exposure and Risk Estimates for ETU from Mancozeb

Residential handler risk estimates are not of concern (MOEs > LOC). MOEs range from 32,700 (mixing/loading/applying liquid formulation to vegetable gardens by backpack) to 130,000 (mixing/loading/applying liquid formulation to vegetable gardens by hose-end sprayer). A summary of ETU non-cancer exposure risk estimates for residential handlers can be found in Table 15.

Combining Exposures/Risk Estimates:

The non-cancer risk calculations for exposures by residential handlers to ETU were calculated in a similar manner as for occupational handlers. Dermal and inhalation risk estimates were combined in this assessment, since the toxicological effects for these exposure routes were similar. ETU dermal and inhalation risk estimates were combined using the following formula:

ETU Total MOE = Point of Departure (mg/kg/day) / Combined dermal + inhalation dose (mg/kg/day)

Table 14: Short-term Residential Handler Non-cancer Exposure and Risk Estimates for Mancozeb.						
Exposure Scenario	**Level of Concern**	**Inhalation Unit Exposure [2]** (mg/lb ai)	**Maximum Application Rate[1]** (lb ai/ft^2)	**Area Treated or Amount Handled Daily[2]**	**Inhalation**	
					Dose (mg/kg/day)[3]	**MOE[4]**
Mixer/Loader/Applicator (Adult Males, Females >49 years)						
Home Gardens, liquid concentrate, Manually-pressurized handwand	30	0.018	5.5×10^{-5}	1200 ft^2	1.35×10^{-5}	1.6×10^{6}
Home Gardens, liquid concentrate, backpack		0.14			1.05×10^{-4}	200,000
Home Gardens, liquid concentrate, Hose-end sprayer		0.0014			1.05×10^{-6}	20×10^{6}
Mixer/Loader/Applicator (Adult Females 13-49 years)						
Home Gardens, liquid concentrate, Manually-pressurized handwand (Females 13-49 years)	300	0.018	5.5×10^{-5}	1200 ft^2	1.57×10^{-5}	1.3×10^{6}
Home Gardens, liquid concentrate, backpack		0.14			1.22×10^{-4}	170,000
Home Gardens, liquid concentrate, Hose-end sprayer		0.0014			1.22×10^{-6}	17×10^{6}

[1] Based on registered label (EPA Reg. 62719-396).
[2] Unit exposure values and estimates for area treated or amount handled based on Exposure Science Advisory Council 2012 Residential SOPs: http://www.epa.gov/pesticides/science/residential-exposure-sop.html
[3]Inhalation Dose = Inhalation Unit Exposure (ug/lb ai) x Conversion Factor (0.001 mg/ug) x Application Rate (lb ai/acre or gal) x Area Treated or Amount Handled (A or gallons/day) / BW (kg).
[4] Inhalation MOE = Inhalation NOAEL (mg/kg/day) / Inhalation Dose (mg/kg/day)

Table 15: Short-term Residential Handler Non-cancer Exposure and Risk Estimates for ETU from Mancozeb.											
Exposure Scenario	Level of Concern	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure [1] (mg/lb ai)	Maximum Application Rate[2] (lb ai/ft^2)	Area Treated or Amount Handled Daily[1]	ETU Dermal Dose (mg/kg/day)[5]		ETU Inhalation Dose (mg/kg/day) [5]		Total ETU Dose (mg/kg/day)[6]	MOE[7]
						ETU from Direct Exposure (Present in Tank Mix) [3]	ETU Metabolized from Mancozeb[4]	ETU from Direct Exposure (Present in Tank Mix) [3]	ETU Metabolized from Mancozeb[4]		
Mixer/Loader/Applicator (Adult Males, Females >49 years)											
Home Gardens, liquid concentrate, Manually-pressurized handwand	100	63	0.018	5.5 x 10^{-5}	1200 ft^2	2.46 x 10^{-5}	3.54 x 10^{-5}	2.7 x 10^{-8}	1.01 x 10^{-6}	6.10 x 10^{-5}	110,000
Home Gardens, liquid concentrate, backpack		130	0.14			5.07 x 10^{-5}	7.31 x 10^{-5}	2.10 x 10^{-7}	7.88 x 10^{-6}	1.32 x 10^{-4}	53,000
Home Gardens, liquid concentrate, Hose-end sprayer		58	0.0014			2.26 x 10^{-5}	3.26 x 10^{-5}	2.10 x 10^{-9}	7.8 x 10^{-8}	5.53 x 10^{-5}	130,000
Mixer/Loader/Applicator (Adult Females 13-49 years)											
Home Gardens, liquid concentrate, Manually-pressurized handwand (Females 13-49 years)	1,000	63	0.018	5.5 x 10^{-5}	1200 ft^2	2.84 x 10^{-5}	4.10 x 10^{-5}	3.13 x 10^{-8}	1.17 x 10^{-6}	7.07 x 10^{-5}	70,600
Home Gardens, liquid concentrate, backpack		130	0.14			5.87 x 10^{-5}	2.12 x 10^{-5}	3.43 x 10^{-7}	9.13 x 10^{-6}	1.53 x 10^{-4}	32,700
Home Gardens, liquid concentrate, Hose-end sprayer		58	0.0014			2.62 x 10^{-5}	3.78 x 10^{-5}	2.43 x 10^{-9}	9.13 x 10^{-8}	6.41 x 10^{-5}	78,000

[1] Unit exposure values and estimates for area treated or amount handled based on ExpoSAC 2012 Residential SOPs: http://www.epa.gov/pesticides/science/residential-exposure-sop.html

[2] Based on registered label (EPA Reg. 62719-396).
Daily Exposure = Unit Exposure (ug/lb ai) x Conversion Factor (0.001 mg/ug) x Application Rate (lb ai/acre or gal) x Area Treated or Amount Handled (A or gal/day) x DAF (%)

[3] ETU Average Daily Dose from Direct Exposure to ETU (mg/kg/day) = [Daily Exposure (mg ai/day) * Absorption (%)]/ BW (kg)
Absorption =0.1 (for mixing and loading) or 0.2 (for application) % of mancozeb.

[4] ETU Average Daily Dose From metabolic conversion of mancozeb (mg/kg/day) = [Daily Exposure (mg ai/day) * Absorption (%)*Metabolic ETU Conversion]/ BW (kg)
7.5 percent of the absorbed mancozeb dose is metabolically converted to ETU

[5] Dermal or Inhalation Dose= ETU Average Daily Dose from Direct Exposure to ETU (mg/kg/day) + ETU Average Daily Dose From metabolic conversion of mancozeb (mg/kg/day)

[6] Total ETU Dose = Total Dermal ETU Dose (mg/kg/day) + Total Inhalation ETU Dose (mg/kg/day)

[7] Total MOE = NOAEL (mg/kg/day)/Total ETU Dose (mg/kg/day). ETU Short-Term Dermal and Inhalation NOAEL: 5 mg/kg/day (females 13-49); 7 mg/kg/day (males, females >49)

Summary of Residential Handler Cancer Exposure and Risk Estimates for ETU from Mancozeb

The cancer risk to home gardeners was reassessed in this document, as they will be used for the aggregate risk assessment. Further description of the assumptions and data used in the assessment may be found in the previous risk assessment. As previously noted, mancozeb's potential for carcinogenicity is due to the formation of the metabolite ETU. Cancer risks from exposure to ETU as a result of application of mancozeb are calculated by estimating exposure to mancozeb-derived ETU and using the ETU Q_1^* of 0.0601 $(mg/kg/day)^{-1}$ to provide a quantitative estimate of risk.

The cancer risk calculations for exposures by residential handlers to ETU were calculated in a similar manner as for occupational handlers with the following assumptions:

Days per year of Exposure
To assess cancer risk, it is assumed that residential handlers would be exposed 5 days per year.

Years per Lifetime of Exposure:
It is assumed that residential handlers would be exposed for 50 years out of a 78-year lifespan.

Lifetime Expectancy:
Life expectancy values are from the Exposure Factors Handbook 2011 Edition Table 18-1 (U.S. EPA, 2011). The table shows that the overall life expectancy is 78 years based on life expectancy data from 2007. In 2007, the average life expectancy for males was 75 years and 80 years for females. Based on the available data, the recommended value for use in cancer risk assessments is 78 years.

The cancer risks for all M/L/A scenarios are estimated in the 10^{-8} range for residential handlers. Residential handler estimated cancer risks were calculated for applicators using a backpack sprayer, manually pressurized and hose-end sprayer. For applicators using backpack sprayers the estimated cancer risk from mancozeb-derived ETU was 7.0×10^{-8}. Residential handlers using manually pressurized sprayers had an estimated cancer risk of 3.2×10^{-8}. Handlers using hose-end sprayers had an estimated cancer risk of 2.9×10^{-8}. A summary of ETU cancer exposure risk estimates for residential handlers can be found in Table 16.

Table 16: Short -Term Residential Handler Cancer Exposure and Risk Estimates for ETU from Mancozeb.						
Crop or Target	Exposure Scenario	Handler Dermal ADD[1] (mg/kg/day)	Handler Inhalation ADD[2] (mg/kg/day)	Total Absorbed Dose ADD (mg/kg/day)	Total LADD [3] (mg/kg/day)[3]	Residential Handler Cancer Risk Estimate[4]
Mixer/Loader/Applicator						
Home Gardens (Vegetables)	Liquid concentrate - Manually-pressurized handwand	6.00×10^{-5}	1.04×10^{-6}	6.10×10^{-5}	5.36×10^{-7}	3.2×10^{-8}
	Liquid concentrate - Backpack	1.24×10^{-4}	8.09×10^{-6}	1.32×10^{-4}	1.16×10^{-6}-	7.0×10^{-8}
	Liquid concentrate - Hose-end sprayer	5.52×10^{-5}	8.09×10^{-8}	5.53×10^{-5}	4.86×10^{-7}	2.9×10^{-8}

[1] Dermal LADD = Dermal dose * Days per year of exposure *Years per lifetime of exposure / (365 days/year x Lifetime expectancy).
[2] Inhalation LADD = Inhalation Dose * Days per year of exposure *Years per lifetime of exposure / (365 days/year x Lifetime expectancy).
[3] Total LADD = total absorbed dose [Dermal dose + Inhalation Dose] * Days per year of exposure * Years per lifetime of exposure / (365 days/year x Lifetime expectancy).
[4] Cancer risk estimates = LADD * Q_1^*, where $Q_1^* = 6.01 \times 10^{-2}$ $(mg/kg/day)^{-1}$.

6.2 Residential Post-application Exposure/Risk Estimates

Mancozeb can be used in areas that can be frequented by the general population including residential areas (e.g., home lawns and gardens) and golf courses. As a result, individuals can be exposed by entering areas that have been previously treated with mancozeb. The detailed assessment for residential exposures may be found in the most recent risk assessment (D327307 & D327318; D. Davis, *et al.*, 6/11/07). An updated assessment of the most representative scenarios to be used in the aggregate assessment is presented below.

As previously mentioned, there are no direct homeowner applications of mancozeb to turf; however, there is a registered sod farm use and the treated sod could be subsequently transplanted to a residential setting. HED considers post-application exposure resulting from this scenario to be negligible for the following reasons: (1) mancozeb has a post-harvest interval (PHI) of 5 days for sod; (2) it is unlikely that sod treated with mancozeb would be installed more than once per year; (3) transplanted sod requires constant and significant watering which will result in decreased mancozeb residues on the transplanted sod; and (4) it is unlikely that adults or children will spend any significant amount of time on recently transplanted sod until it is rooted which typically occurs around 2 weeks after transplanting. Therefore, dermal and incidental oral post-application scenarios were not assessed for the sod farm use of mancozeb.

The quantitative exposure/risk assessment for residential post-application exposures is based on: home gardeners applying mancozeb to vegetables and golfers contacting mancozeb treated turf after application. As no dermal hazard was identified for mancozeb, a quantitative dermal post-application assessment (non-cancer and cancer) was only performed for its metabolite, ETU.

The lifestages selected for each post-application scenario are based on an analysis provided as an Appendix in the 2012 Residential SOPs (http://www.epa.gov/pesticides/science/residential-exposure-sop.html). These lifestages are not the only lifestages that could be potentially exposed for these post-application scenarios; however, the assessment of these lifestages is health protective for the exposures and risk estimates for any other potentially exposed lifestages.

Residential Post-application Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the residential post-application risk assessment. Each assumption and factor is detailed in the 2012 Residential SOPs (http://www.epa.gov/pesticides/science/residential-exposure-sop.html and in Appendix A of this document.

Residential Post-application Non-Cancer Exposure and Risk Equations

The algorithms used to estimate residential post-application exposure and dose can be found in the 2012 Residential SOPs (http://www.epa.gov/pesticides/science/residential-exposure-sop.html) and in Appendix A of this document.

6.2.1 Post-application Inhalation

Based on the Agency's current practices, a quantitative post-application inhalation exposure assessment was not performed for mancozeb or its metabolite ETU at this time. However, volatilization of pesticides may be a potential source of post-application inhalation exposure to individuals nearby to pesticide applications. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP) in December 2009. The Agency received the SAP's final report on March 2, 2010 (http://www.epa.gov/scipoly/SAP/meetings/2009/120109meeting.html). The Agency is in the process of evaluating the SAP report and may, as appropriate, developing policies and procedures, to identifying the need for and, subsequently, the way to incorporate post-application inhalation exposure into the Agency's risk assessments. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative post-application inhalation exposure assessment for mancozeb.

6.2.2 Post-application Dermal

6.2.2.1 Home Garden Post-application Scenarios

Table 17, below summarizes the post application non-cancer risks estimates from mancozeb-derived ETU for adults and youth (children 6 to 11 years old) exposed to treated home gardens on Day 0 (the day of application). Exposures are shown for the commodity that might be found in a home garden and led to the highest exposure (*i.e.,* cucurbit vegetables). MOEs for both subpopulations on Day 0 exceed the LOCs (*i.e.,* MOE ≥ 1000 for adults and MOE ≥ 100 for youth), therefore; are not of concern.

Table 17. Mancozeb-derived ETU Post-application Non- Cancer Exposure and Risk Estimates for Adult and Youth Home Gardeners [1]

Lifestage	LOC	Crop Group	Application Rate (lb ai/acre)	Initial DFR (ug/cm^2) [2]		TC (cm2/ hr)	ETU Foliar Dose (mg/kg/day)	Mancozeb Metabolized Dose to ETU (mg/kg/day)	Total Absorbed Dermal Dose (mg/kg/day)	MOE
				Mancozeb	ETU					
Adult (Female 13-49 years old)	1000	Vegetable, cucurbit – West [2]	2.4	6.77	0.01	8,400	0.0007	0.0012	0.0019	**2,700**
Adult (males, females >49 years old)	100					8,400	0.0006	0.0010	0.0016	**4,300**

Table 17. Mancozeb-derived ETU Post-application Non- Cancer Exposure and Risk Estimates for Adult and Youth Home Gardeners [1]

Lifestage	LOC	Crop Group	Application Rate (lb ai/acre)	Initial DFR (ug/cm^2) [2]		TC (cm2/ hr)	ETU Foliar Dose (mg/kg/day)	Mancozeb Metabolized Dose to ETU (mg/kg/day)	Total Absorbed Dermal Dose (mg/kg/day)	MOE
				Mancozeb	ETU					
6 to 11 yrs old	100					4,600	0.0004	0.0008	0.0012	**5,800**
11 to <16 years (except females 13-16 years old)	100					8,400	0.000843	0.001419	0.002262	**3,100**

[1] Exposures are shown for high contact activities for the commodity that might be found in a home garden and led to the highest exposure.
[2] Note – while the application rates are the same for west and east cucurbit, the dislodgeable foliar residues for east and west are different. Since west DFR are higher, exposures and risks were estimated for "west" only. Mancozeb study: MRID 44959306. ETU study: MRID 44959603

Post application cancer risks estimates from mancozeb-derived ETU for adults exposed to treated home gardens on Day 0 (the day of application) are summarized in Table 18, below. As in the table above, only the scenario with the highest risk was assessed. Post-application cancer risks for adult home gardeners are estimated in the 10^{-7} range.

Table 18. Mancozeb-derived ETU Post-application Cancer Exposure and Risk Estimates for Adult Gardeners on Day 0 Assuming Five Exposure Days per Year Over a Lifetime

Crop Group	Application Rate (lb ai/acre)[1]	Dose		Cancer Risk [5]
		Total Absorbed Dermal Dose [3] (mg/kg/day)	Lifetime Average Daily Dose (LADD) [4], (mg/kg/day)	
Vegetable, cucurbit – (West)	2.4 [2]	0.0019	1.41×10^{-5}	**8.5×10^{-7}**

[1] Exposures are shown for high contact activities for the commodity that might be found in a home garden and led to the highest exposure.
[2] Note – while the application rates are the same for west and east cucurbit, the dislodgeable foliar residues for east and west are different. Since west DFR are higher, exposures and risks were estimated for "west" only. Mancozeb study: MRID 44959306. ETU study: MRID 44959603
[3] ADD = Absorbed Daily Dose from foliar an metabolized sources of ETU exposure
[4] LADD = Lifetime Average Daily Dose = ADD * (5 exposure days per year/365 days per year)*(50 years of exposure/78 years of life)
[5] Risk = (LADD * Q_1*), where Q_1* = 0.0601 $(mg/kg/day)^{-}$

6.2.2.2 Treated Turf Post-application Scenarios

Adults and children may be exposed to mancozeb-derived ETU through dermal contact with turf treated directly with mancozeb. The scenarios, routes of exposure and lifestages assessed include:

- Golfing: adults (dermal), children 11 < 16 years old (dermal), and children 6 < 11 years old (dermal),

The assumptions for the residential golfer assessment are refined as follows:

- Golfer assessment is based on a maximum application rate of 17.4 lb ai/A (registered label EPA Reg No. 62719-402).
- Golfers have been assessed using a transfer coefficient of 5,300 cm^2/hour. It is assumed golfers wear T-shirt and shorts.
    - The TC is based on a study: *Determination of Dermal and Inhalation Exposure to Reentry Workers During Maintenance Activities in Golf Courses*" (MRID# 46734001). The transfer coefficients used for the "golfer" dermal scenarios were derived using the best available data collected during a golf course maintenance study considered to provide the best representation of the exposures that might be experienced by golfers. The use of the cup changing component from a golf course maintenance study is an acceptable surrogate for golfer exposure because it is assumed that a golfer's highest exposures are most likely to occur when contacting residues from turf on and around the greens and residues remaining on the golf ball. The actions associated with cup changing in the golf course maintenance study are similar to typical golfer actions and, as a result, the actions should result in similar exposures.
- Measured Turf Transferable Residues (TTR) values based on a chemical specific (mancozeb) turf study: MRID 44958501.
    - For golfer non-cancer risk assessment the highest measured residues from the turf study were used: mancozeb initial TTR of 0.20 (ug/cm^2); ETU initial TTR of 0.003 (ug/cm^2).
    - For golfer cancer risk assessment the average highest TTR values (NC, PA, and CA sites) for Mancozeb and ETU residues from the turf study were used: mancozeb TTR of 0.15 (ug/cm^2); ETU TTR of 0.003 (ug/cm^2).
- For golfer non-cancer and cancer risk assessment it was assumed that the tees, greens and fairways are treated and that the exposure time per day would be four hours.
- For cancer risk assessment the exposure days per year is assumed to be **one** based upon the following:
    - Golfers play an average of 19 rounds per year based upon information from the National Golf Foundation for the years 1994 through 2003.
    - According to BEAD, 20% percent of golf courses in the U.S. use mancozeb.
    - According to the Golf Course Superintendent's Association, fungicides are applied to golf courses an average of 6 times per year.

Summary of Non-Cancer Exposure and Risk Estimates for ETU from Mancozeb for Golfers

The MOE for short-term dermal risk for young golfers 6 to <16 years old exposed to ETU from contact with mancozeb treated golf courses is above the LOC of 100 and therefore, is not of concern. The MOE for short-term dermal risk for adult golfers (females 13-49) is above the LOC of 1000 and therefore, is not of concern. A summary of exposure and risk estimates for adults and children exposed to ETU from contact with mancozeb treated golf courses is summarized in Table 19.

Summary of Cancer Exposure and Risk Estimates for ETU from Mancozeb for Golfers

The cancer risk to adult golfers from exposure to mancozeb-derived ETU is estimated in 2.5 x 10^{-8} (tees, greens and fairways). A summary of cancer exposure and risk estimates for adults and children exposed to ETU from contact with mancozeb treated golf courses is summarized in Table 20.

Table 19. Mancozeb-derived ETU Post-application Non-cancer Exposure and Risks Estimates for Golfers [1]											
Lifestage	**LOC**	**Application Rate [2] (lb ai/acre)**	**Mancozeb TTR (ug/cm^2)**	**ETU TTR (ug/cm2)**	**Transfer Coefficient [3] (cm^2/hr)**	**Hours per Day Exposure**	**Mancozeb Dermal Dose [4] (mg/kg/day)**	**Mancozeb Metabolized to ETU Dose [5] (mg/kg/day)**	**ETU Foliar Dose [6] (mg/kg/day)**	**Total ETU absorbed Dose [7] (mg/kg/day)**	**ETU Dermal MOE [8]**
Adult (Female 13-49 years old)	1000	17.4	0.20	0.003	5,300	4.	0.000614	0.000046	0.000239	0.000286	17,500
11 to <16 years (except females 13-16 years old)	100				4,400	4	0.000618	0.000046	0.000240	0.000287	24,400
6 to <11 years	100				2,900	4	0.000725	0.000054	0.000282	0.000337	20,700
Adult (males, females >49 years old)	100				5,300	4	0.000529	0.000040	0.000206	0.000246	28,000

1. Based on Mancozeb initial TTR of 0.20 (ug/cm^2) and ETU initial TTR of 0.003 (ug/cm^2). Highest residue values from turf study: MRID 449585-01.
2. Based on registered label EPA Reg No. 62719-402.
3. Transfer Coefficient (TC) values based on ExpoSAC 2012 Residential SOPs: http://www.epa.gov/pesticides/science/residential-exposure-sop.html
4. Mancozeb Dermal Dose = [DFR ($\mu g/cm^2$) × Transfer Coefficient × 0.001 mg/µg × 4 hrs/day × dermal absorption (%)] ÷ BW (kg)
5.Mancozeb Metabolized Dose to ETU= Mancozeb Dermal Dose × 0.075
6. ETU Foliar Dermal Dose = [DFR ($\mu g/cm^2$) × Transfer Coefficient × 0.001 mg/µg × 4 hrs/day × dermal absorption (%)] ÷ BW (kg).
7. Total Dermal Dose = ETU Foliar Dermal Dose + ETU Metabolized Dose to ETU
8.Total MOE = NOAEL (mg/kg/day)/Total ETU Dose (mg/kg/day). ETU Short-Term Dermal NOAEL: 5 mg/kg/day (females 13-49); 7 mg/kg/day (males, females >49, and youth 6 to <16 except females 13-49).

Table 20. Summary of ETU Post-application Cancer Risks for Adults Exposed to Turf										
Activity	**Application Rate (lb ai/acre)**	**Mancozeb TTR [1] (ug/cm2)**	**ETU TTR (ug/cm2)**	**Transfer Coefficient (cm^2/hr)**	**Hours per Day Exposure**	**Days Per Year Exposure**	**Years of Exposure per Lifetime**	**ADD [2] Total ETU absorbed Dose (mg/kg/day)**	**LADD [3] (mg/kg/day)**	**Cancer Risk [4]**
Golf (Tees, Greens and Fairways)	17.4	0.15	0.03	5,300	4.0	1	50	0.000237	4.1×10^{-7}	2.5×10^{-8}

[1] Average highest TTR valuess (NC, PA, and CA sites) for Mancozeb and ETU residues from turf study: MRID 449585-01)
[2] ADD = Absorbed Daily Dose from foliar an metabolized sources of ETU exposure
[3] LADD = Lifetime Average Daily Dose = ADD * (1 exposure day per year/365 days per year)*(50 years of exposure/78 years of life)
[4] Risk = (LADD * Q_1*), where Q_1* = 0.0601 $(mg/kg/day)^{-1}$

6.2.2.3 Summary of Short-Term Residential Post-application Non-cancer Exposure and Risk Estimates for ETU from Mancozeb

A summary of short-term residential post-application exposure and risk estimates for ETU from mancozeb identified is presented on Table 21.

Table 21. Summary of Short-Term Residential Post-application Non-cancer Exposure and Risk Estimates for ETU from Mancozeb

Lifestage	Post-application Exposure Scenario			Dose (mg/kg/day)	LOC	MOEs
Adult (Female 13-49 years old)	Liquid sprays	Dermal	Home Garden Activities	**0.0019**	**1000**	**2700**
			Golfing	.000286	1000	17,500
Adult (Male, female >49 years old)		Dermal	Home Garden Activities	0.0016	100	4,300
			Golfing	0.000246	100	28,000
Child 11 < 16 years old (except females 13-16 years old)		Dermal	Home Garden Activities	0.002262	100	3,100
			Golfing	0.000287	100	24,400
Child 6 < 11 years old		Dermal	Home Garden Activities	0.0012	100	5,800
		Dermal	Golfing	0.000337	100	20,700
Child 1 < 2 year old		Dermal	NA	NA	1000	NA
		Hand to Mouth		NA	1000	NA
		Object to Mouth		NA	1000	NA
		Soil Ingestion		NA	1000	NA

6.3 Recommendations for Aggregate Assessment

HED combines risk values resulting from separate exposure scenarios when it is likely they can occur simultaneously based on the use pattern and the behavior associated with the exposed population. For home garden scenarios a combined residential exposure assessment for handlers was conducted for ETU exposures. The residential handler scenario identified for use in performing an aggregate exposure assessment was for adults treating home gardens with mancozeb formulations (mixing/loading/application) utilizing a backpack sprayer (ETU combined MOE=32,700). However, for mancozeb exposures, the only route of exposure for handlers was through the inhalation route, therefore; the residential handler scenario identified for use in performing an aggregate exposure assessment was for home gardeners applying mancozeb to vegetables utilizing a backpack sprayer (MOE=170,000). A summary of short-term residential handler exposure and risk estimates for mancozeb inhalation exposures and ETU combined exposures is presented on Tables 22 and 23, respectively.

The residential post-application scenarios identified for use in performing an aggregate exposure assessment were adults (MOE=2,700), children 11 to <16 years old (MOE=3,100), and children 6 to < 11years old, (MOE=5,800) exposed to treated home gardens. A summary of short-term residential post-application exposure and risk estimates for ETU from mancozeb identified for use in performing an aggregate exposure assessment is presented on Table 24**.**

Table 22. Residential Exposures for the Mancozeb Aggregate Assessment (Residential Handler/Garden Use)

Lifestage	Exposure Scenario			Dose (mg/kg/day)	LOC	MOEs
Adult (Female 13-49 years old)	M/L/A Backpack sprayer	Inhalation	Home Garden Activities	0.000122	300	170,000
Adult (Male, female >49 years old)	M/L/A Backpack sprayer	Inhalation	Home Garden Activities	0.000105	30	200,000

Table 23. Residential Exposures for the ETU from Mancozeb Aggregate Assessment (Residential Handler/Garden Use)

Lifestage	Exposure Scenario			Dose (mg/kg/day)	LOC	MOEs
Adult (Female 13-49 years old)	M/L/A Backpack sprayer	Combined (Inhalation + Dermal)	Home Garden Activities	0.000153	1000	32,700
Adult (Male, female >49 years old)	M/L/A Backpack sprayer	Combined (Inhalation + Dermal)	Home Garden Activities	0.000132	100	37,900

Table 24. Residential Exposures for the ETU from Mancozeb Aggregate Assessment (Post-Application Exposures/Garden Use)

Lifestage	Post-application Exposure Scenario	Dose (mg/kg/day)	LOC	MOEs

Table 24. Residential Exposures for the ETU from Mancozeb Aggregate Assessment (Post-Application Exposures/Garden Use)						
Lifestage	Post-application Exposure Scenario			Dose (mg/kg/day)	LOC	MOEs
Adult (Female 13-49 years old)	Liquid sprays	Dermal	Home Garden Activities	0.0019	1000	2,700
Child 6 < 11 years old				0.0012	100	5,800
Child 11 < 16years old				0.00226	100	3,100

The residential handler scenario identified for use in performing an aggregate cancer assessment was for home gardeners applying mancozeb to vegetables utilizing a backpack sprayer. For applicators using backpack sprayers the estimated cancer risk from mancozeb-derived ETU was 7.0×10^{-8} (Table 25).

Table 25. Residential Exposures for the ETU from Mancozeb Aggregate Cancer Assessment (Residential Handler/Garden Use).			
Crop or Target	Total Absorbed Dose ADD (mg/kg/day)	Total LADD [3] (mg/kg/day)[3]	Residential Handler Cancer Risk Estimate[4]
Mixer/Loader/Applicator (Liquid concentrate – Backpack Sprayer)			
Home Gardens (Vegetables)	1.32×10^{-4}	1.16×10^{-6}-	**7.0×10^{-8}**

The residential post-application scenario identified for use in performing an aggregate cancer assessment was for adults exposed to treated home gardens. The cancer risk to adult gardeners from exposure to mancozeb-derived ETU is estimated in 8.5×10^{-7} (Table 26).

Table 26. Residential Exposures for the ETU from Mancozeb Aggregate Cancer Assessment (Post-Application Exposures/Garden Use)			
Activity	ADD Total ETU absorbed Dose (mg/kg/day)	LADD (mg/kg/day)	Cancer Risk
Home Garden Activities	0.0019	1.41×10^{-5}	8.5×10^{-7}

7.0 REFERENCES

Mancozeb: Occupational and Residential Risk Assessment to Support Request for Section 3 Registrations on Walnuts. D405401, A. Rivera-Lupiáñez, 11/04/12.

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8.0 APPENDIX A
Summary of Residential Handler and Post-application Algorithms

1.0 Residential Handlers

1.1 Residential Handler Exposure Calculations

1.1.1 Turf, Gardens and Trees

Dermal and Inhalation Handler Exposure Algorithm

Daily dermal and inhalation exposure (mg/day) for residential pesticide handlers, for a given formulation-application method combination, is estimated by multiplying the formulation-application method-specific unit exposure by an estimate of the amount of active ingredient handled in a day, using the equation below:

$E = UE * AR * A$

where:

E = exposure (mg/day);
UE = unit exposure (mg/lb ai);
AR = application rate (e.g., lb ai/ft^2, lb ai/gal); and
A = area treated or amount handled (e.g., ft^2/day, gal/day).

1.2 Residential Handler Dose Calculations

Dermal and/or inhalation absorbed doses normalized to body weight are calculated as:

$D = E * AF / BW$

where:

D = dose (mg/kg-day);
E = exposure (mg/day);
AF = absorption factor (dermal and/or inhalation); and
BW = body weight (kg).

2.0 Residential Post-application

2.1 Turf/Golfing

Post-application Dermal Exposure Algorithm – Golfing

Exposure resulting from contacting previously treated turf while golfing is calculated as follows:

$$E = TTRt * CF1 * TC * ET$$

where:

E = exposure (mg/day);
TTR_t = turf transferable residue on day "t" (µg/cm^2);
CF1 = weight unit conversion factor (0.001 mg/µg);
TC = transfer coefficient (cm^2/hr); and
ET = exposure time (hr/day).

and

$$TTRt = AR * F * (1-F_D)^t * CF2 * CF3$$

where:

TTR_t = turf transferable residue on day "t" (µg/cm^2);
AR = application rate (lbs ai/ft^2 or lb ai/acre);
F = fraction of ai retained on turf (unitless);'
F_D = fraction of residue that dissipates daily (unitless);
t = post-application day on which exposure is being assessed;
CF2 = weight unit conversion factor (4.54 x 10^8 µg/lb); and
CF3 = area unit conversion factor (1.08 x 10^{-3} ft^2/cm^2 or 2.47 x 10^{-8} acre/cm^2).

Absorbed dose, normalized to body weight, is calculated as:

$$D = \frac{E * AF}{BW}$$

where:

D = dose (mg/kg-day);
E = exposure (mg/day);
AF = absorption factor (dermal); and
BW = body weight (kg).

Table A-1: Turf (Golfing) – Inputs for Residential Post-application Dermal Exposure			
Algorithm Notation	**Exposure Factor (units)**		**Point Estimate(s)**
AR	Application rate (mass active ingredient per unit area)		17.4 lb ai/A
F	Fraction of AR as TTR following application	L/WP/WDG	0.01
F_D	Daily residue dissipation	L/WP/WDG	0.1
TC	Transfer Coefficient (cm^2/hr)	Adult	5,300
		Children 11 < 16 years old	4,400
		Children 6 < 11 years old	2,900
ET	Exposure time (hours per day)	Pesticides used on greens, tees, and fairways	4
		Pesticides used only on greens and tees	1
BW	Body Weight (kg)	Adults	69
		Children 11 < 16 years old	57
		Children 6 < 11 years old	32
NA = not applicable L/WP/WDG = liquid/wettable powder/water dispersible granule			

2.2 Home Gardens

Post-application Dermal Exposure Algorithm

Exposure resulting from contacting previously treated gardens and trees while performing physical activities is calculated as shown below. Residential post-application exposure assessment must include calculation of exposure on the day of application. Therefore, though an assessment can present exposures for any day "t" following the application, it must include "day 0" exposure.

$$E = DFR_t * CF1 * TC * ET$$

where:

E = exposure (mg/day);
DFR_t = dislodgeable foliar residue on day "t" (µg/cm^2);
CF1 = weight unit conversion factor (0.001 mg/µg);
TC = transfer coefficient (cm^2/hr); and
ET = exposure time (hrs/day).

In the absence of chemical-specific data, DFR_t can be calculated as follows:

$$DFR_t = AR * F_{AR} * (1\text{-}F_D)^t * CF2 * CF3$$

where:

DFR_t = dislodgeable foliar residue on day "t" (µg/cm^2);
AR = application rate (lbs ai/ft^2 or lb ai/acre);
F_{AR} = fraction of ai as dislodgeable residue following application (unitless);
F_D = fraction of residue that dissipates daily (unitless);
t = post-application day on which exposure is being assessed;
CF2 = weight unit conversion factor (4.54 x 10^8 µg/lb); and
CF3 = area unit conversion factor (1.08 x 10^{-3} ft^2/cm^2 or 2.47 x 10^{-8} acre/cm^2).

Absorbed dermal dose, normalized to body weight, is calculated as:

$$D = \frac{E * AF}{BW}$$

where:
D = dose (mg/kg-day);
E = exposure (mg/day);
AF = absorption factor (dermal and/or inhalation); and
BW = body weight (kg).

Table A-2: Home Gardens–Inputs for Residential Post-application Dermal Exposure					
Algorithm Notation	**Exposure Factor (units)**				**Point Estimate(s)**
AR	Application rate (mass ai per unit area)				2.4 lb ai/A
F_{AR}	DFR following application, if chemical-specific is unavailable (fraction)				0.25
F_D	Daily residue dissipation, if chemical-specific is unavailable (fraction)				0.10
TC	Transfer Coefficient (cm^2/hr)	Gardens[a]	Adults		8400
			Children 6 < 11 years old		4600
ET	Exposure Time (hours per			Adults	2.2
	day)	Home activities[b]	Gardens	Children 6 < 11 years old	1.1

Table A-2: Home Gardens–Inputs for Residential Post-application Dermal Exposure			
Algorithm Notation	**Exposure Factor (units)**		**Point Estimate(s)**
BW	Body weight (kg)	Adults	69
		Children 6 < 11 years old	32
[a] Transfer coefficient point estimates from a composite distribution assuming equal proportion of time spent conducting various activities. See "Transfer Coefficient" section below. Children 6 < 11 years old TC derived using surface area adjustment (see *Section 2.3* of the 2012 Residential SOPs). [b] Activity time point estimates from a composite distribution assuming equal proportion of each respective activity. Time for children 6 < 11 years old derived using hrs/day ratio adjustment.			